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Stereocontrolled allylation of 2-amino-2-deoxy sugar derivatives by a free-radical procedure [1]

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Abstract

Preparative routes for anomerically specific 1-*C*-allylation of 2-amino-2-deoxy sugars have been evaluated in a comparative study of various *N*-substituents and aglycons as precursors for glycosyl radicals that effectively capture an allyl group from allyltributyltin. The crystalline triacetate **4** of 3-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-1-propene (**6**) was obtained in 70% yield when 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**1**) was treated with allyltributyltin under free-radical conditions, whereas the corresponding bromide **3** led only to an oxazolidine derivative; the β-1-ethylxanthate analogue of **1** gave **4**, but in only 25% yield. The 2-trifluoroacetamido 1-bromide analogue of **1** was also an effective radical source, giving the 2-trifluoroacetamido analogue **8** of **4** in 60% yield. The free amino analogue **7** of **4** was conveniently obtained via the 2-*p*-methoxybenzylideneamino 1-bromide analogue of **1**. Use of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide as radical precursor allowed stereospecific access to β-1-*C*-allyl derivatives of the amino sugar. The crystalline galactosamine analogue **12** of **4** was obtained by using the *galacto* analogue of chloride **1**, but the corresponding *manno* chloride gave only an oxazoline product. The 1-*C*-allylated amino sugar derivatives are conformationally more mobile than derivatives not having a 1-*C*-linked substituent.

Keywords: *C*-Glycosyl derivatives; 2-Amino sugars; Free-radical reactions; Glycosyl radicals

1. Introduction

1-*C*-Linked glycosyl derivatives (often termed, incorrectly, '*C*-glycosides'), formed when the anomeric oxygen atom of a glycoside is replaced by a carbon atom, have received much attention during the past decade. They occur as subunits in a variety of natural products [2] and act as enzyme inhibitors [3]. Because they are stable toward both acidic and enzymic hydrolysis, there is high interest in the use of *C*-linked disaccharides for enzymic and metabolic studies [4]. *C*-Linked glycosyl compounds also serve as useful chiral synthons for organic synthesis [5]. A wide range of methods for carbon–carbon bond formation at the anomeric carbon of neutral sugars has been developed [6–8].

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The most important of these include the Lewis acid-catalyzed nucleophilic addition [6] and radical-promoted addition [7] to the anomeric center of an appropriately activated carbohydrate derivative.

The importance of amino sugars as constituents of aminoglycoside antibiotics, antigenic determinants, glycoproteins, and glycolipids is well recognized. Analogues linked through carbon at C-1 may constitute useful glycomimetics, stable to glycoprocessing enzymes. However, synthetic access to these structures is limited by the difficulty of preparing such carbon-linked analogues of 2-amino-2-deoxy sugars. The Lewis acid-catalyzed *C*-glycosylation of suitably activated sugar derivatives fails for 2-amino-2-deoxy sugars [6b], presumably because the nitrogen atom binds the acid catalyst. Few examples of successful synthesis of 2-amino-2-deoxy *C*-glycosyl derivatives have been reported [9]. The first such instance, ethyl 2-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)acetate, was prepared through a Wittig reaction of 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranose with (ethoxycarbonylmethylene)triphenylphosphorane, followed by a Michael addition reaction [9a,b]. Nicotra and co-workers reported that an α-*C*-glycosyl derivative of 2-amino-2-deoxy-D-glucose can be produced stereoselectively through the reaction of (2,3,5-tri-*O*-benzyl-D-arabinofuranosyl)benzylamine with vinylmagnesium bromide and subsequent mercuriocyclization of the open-chain product thereby obtained [9c]. A different approach has been described that involves the hetero [4+2] cycloaddition of azo compounds with a 1-alkylglucal and subsequent conversions [9d]. Bertozzi and Bednarski reported the synthesis of 2-azido-2-deoxy-α-*C*-glycosyl compounds by the direct Lewis acid-catalyzed addition of alkylsilanes to 2-azido-2-deoxyglycosyl nitrates [9e] (compare ref. [9g]). A C-2 oxidation, oximation, reduction sequence performed on a *C*-glycosyl derivative of a neutral sugar provides access to *C*-glycosyl derivatives of 2-amino-2-deoxy-D-glucose and -mannose, as recently reported by Nicotra and co-workers [9k]. Coupling of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride with potassium diethylmalonate was shown by Kim and Hollingsworth [9h] to give a β-*C*-alkylated product in 21% yield. A novel and potentially generally useful approach involves reaction of a lithiated dianion derived from 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose with various electrophiles [9i].

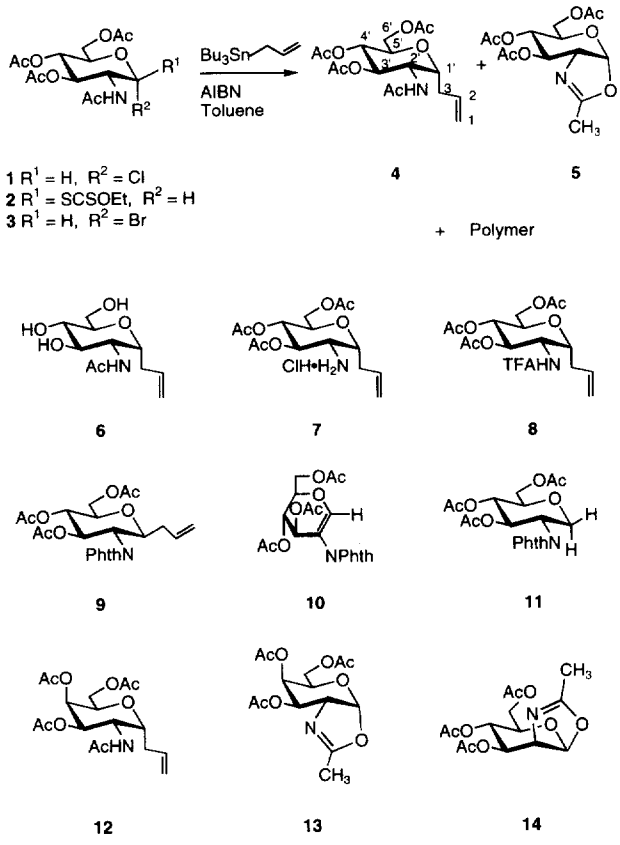
The methods published thus far for the synthesis of 2-amino-2-deoxy-*C*-glycosyl compounds mostly suffer the disadvantages of several steps, expensive starting materials, and low stereoselectivity. We first reported in 1992 the stereocontrolled α- and β-allylation of 2-amino-2-deoxy sugars at the anomeric center through a free-radical allylation reaction [1a]. The free-radical allylation reaction of suitably activated 2-amino-2-deoxy sugars has the advantages of few steps, high stereoselectivities, and the use of inexpensive and abundant natural amino sugars. Bertozzi and co-workers published related experimental results for the synthesis of β-*C*-glycosyl derivatives of *N*-acetylglucosamine in 1996 [9j].

In this paper we provide a full report of our research [1] on the introduction, highly stereoselectively, of a C–C bond at the anomeric center of 2-amino-2-deoxy sugar derivatives by a free-radical procedure. The course of the free-radical reaction, and the influence on product yield and stereochemical outcome of different protecting groups on the amino function and substituents at the anomeric center, is evaluated in detail.

2. Results and discussion

The stereocontrolled synthesis of 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1-propene (**4**) was achieved by treating 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride [10] (**1**) with allyltributyltin (3 mol equiv) in the presence of the radical initiator AIBN (0.15 mol equiv) in dry toluene for 8 h at 85 °C under argon. Purification on a column of silica gel provided **4** as a white solid in 67% yield. Recrystallization from 3:1 hexanes–ethyl acetate afforded white needles having mp 109–110 °C, $[\alpha]_D$ +47° in chloroform. The β anomer of **4** was detected by NMR methods, formed in 2% yield, although it could not be obtained pure through conventional recrystallization and chromatography of the mother liquor. Polymerization was the major competing reaction and a polymeric material was obtained in 24% yield. The mass spectrum of the polymer showed peaks for the mass of a dimer and a trimer of the *C*-glycosyl derivative **4**. The oxazoline **5** was a side-product, isolated in 5% yield.

The preparation was readily conducted on a 10-gram scale. The best yield was obtained when the



starting material, 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride, was freshly prepared. The yield of product **4** was increased from 40 to 67% by increasing the amount of allyltributyltin from 2 to 3 molar equivalents. When the amount of initiator (AIBN) was decreased from 0.15 to 0.075 mol equiv, the yield was decreased from 67 to 26%. When the volume of toluene solvent was doubled, the yield decreased from 67 to 49%.

Assignment of the structure of **4** was based on its satisfactory elemental analysis, NMR spectra, specific optical rotation, and mass spectrum. The α-anomeric configuration of **4** was assigned on the basis of the small $J_{1',2'}$ value (4.5 Hz) and a lower downfield chemical shift of H-1′ (at δ 4.21) as compared with the large $J_{1',2'}$ value of 10.1 Hz and higher upfield chemical shift of H-1′ (at δ 3.16) for the β anomer of **4**. The ^{1}H NMR spectrum of **4** showed an apparent quintet (ddd, *J* 4.5, 4.8, 10.0 Hz) for H-1′ at δ 4.21 and a doubled doublet of doublets (*J* 4.5, 8.2, 8.7 Hz) for H-2′ at δ 4.52. The relatively small values of $J_{2',3'}$, $J_{3',4'}$, and $J_{4',5'}$ (8.2, 6.8, and 6.8 Hz) for compound **4** in C_6D_6 suggest that this glycosylalkene does not exclusively adopt the $^4C_1$ conformation, but exists in conformational equilibrium [11] between the $^4C_1$ and $^1C_4$ conformers, with the former being preponderant.

The influence of different substituents at the anomeric center of 2-amino-2-deoxy sugars on the course and stereoselectivity of the free-radical reaction was investigated. 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl ethylxanthate [12] (**2**) in toluene was treated with 2 molar equivalents of allyltributyltin and 0.15 molar equivalent of AIBN at 80 °C overnight under argon. The procedure afforded the same glycosylalkene **4**, but in only 25% yield. Other products could not be purified and identified.

The 1-ethylxanthate substituent was thus not as effective as the 1-chloride group for the production of glycosyl radicals, and it took overnight reaction for the starting material **2** to be consumed. Precursors **1** and **2** both have the same 2-substituent, but the α-substituted chloride and the β-substituted xanthate each give rise to the same α-*C*-glycosyl product, indicating that the stereoselectivity at the anomeric center during the free-radical reaction is evidently not influenced by the configuration of the activating group on the anomeric center in the precursor, at least when the same protecting group was present on the amino function.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide [13] (**3**) was also evaluated as a possible free-radical precursor. However, under reaction conditions similar to those successfully used with chloride **1** to produce the α-*C*-glycosyl product **4**, compound **3** gave the oxazoline derivative **5** as the major product (88% yield), and the *C*-allylated compound **4** could not be found in the reaction mixture. The excellent leaving-group character of bromide can be expected to generate a transient oxonium ion that is rapidly stabilized through participation by the acetamido group, with a 1,2-cyclization reaction leading to the oxazoline product **5**. In contrast, chloride is a less effective leaving group, and production of an intermediate glycosyl radical rather than an oxonium ion is the favored pathway, leading to the radical-capture product **4** as the major product, with the oxazoline **5** being obtained in only 5% yield.

Deacetylation of **4** with a catalytic amount of sodium methoxide in methanol gave 3-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-1-propene (**6**) in quantitative yield; recrystallized from ethanol it

was obtained as white crystals having mp 204–206 °C and $[\alpha]_D$ +109° in methanol.

The influence of the amino protecting group on the free-radical reaction was studied with three additional *N*-substituents. Treatment of 3,4,6-tri-*O*-acetyl-2-*p*-methoxybenzylideneamino-2-deoxy-α-D-glucopyranosyl bromide [14] with allyltributyltin (3 mol equiv) and AIBN (0.30 mol equiv) for 24 h at 85 °C under argon afforded 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-*p*-methoxybenzylideneamino-α-D-glucopyranosyl)-1-propene. The *N*-substituent was then cleaved by hydrolysis in acidified acetone to give 3-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl)-1-propene hydrochloride (**7**) in 45% yield as a crystalline white solid, mp 220–222 °C (dec), $[\alpha]_D$ +59° in methanol; the corresponding free base was a syrup. The α-anomeric configurational assignment of **7** was based on the small $J_{1',2'}$ coupling constant of 4.8 Hz. The ^{1}H NMR spectrum of **7** showed the N-H signal at the lowest field (δ 8.66) as a very broad singlet. The H-1′ signal appeared at δ 4.44 as a doubled doublet of doublets ($J_{1',2'}$ 4.8 Hz, $J_{1',3a}$ 10.5 Hz, $J_{1',3b}$ 4.9 Hz) and H-2′ at δ 3.79 as a doubled doulet ($J_{1',2'}$ 4.8 and $J_{2',3'}$ 8.8 Hz). The coupling constants of compound **7** showed that the compound in chloroform solution exists essentially in the $^4C_1$ chair conformation ($J_{1',2'}$ 4.8 Hz, $J_{2',3'}$ 8.8 Hz, $J_{3',4'}$ 7.9 Hz, and $J_{4',5'}$ 8.0 Hz).

The strongly electron-withdrawing character of the trifluoromethyl group can be expected to greatly diminish the neighboring-group participatory effect of the amino function in a trifluoroacetyl protecting group as compared with the acetamido group. This consideration made 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide attractive as a possible free-radical precursor, as compared with 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide (**3**), which produced exclusively the oxazoline **5** through 1,2-cyclization during the attempted free-radical allylation reaction. The reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide [15] with allyltributyltin (2 mol equiv) and AIBN (0.15 mol equiv) in dry toluene under argon for 6 h at 85 °C gave the desired product, 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl)-1-propene (**8**) in 60% yield, after chromatographic purification on a column of silica gel. The β anomer of **8** was produced in about 5% yield in the crude product, but it could not be obtained pure. Dissolution of the crude product in hot 4:1 hexanes–ethyl acetate and collecting the initially precipitated syrup afforded pure compound **8** as a colorless syrup, which had $[\alpha]_D$ +22° in chloroform; the β anomer of **8** remained in solution along with additional **8**.

The ^{1}H NMR spectrum of **8** in C_6D_6 showed quite unusual ^{1}H–^{1}H coupling constants for the hydrogen atoms in the tetrahydropyran ring ($J_{1',2'}$ 3.8 Hz, $J_{2',3'}$ 6.0 Hz, $J_{3',4'}$ 5.8 Hz, and $J_{4',5'}$ 4.6 Hz). The anomeric configuration of **8** could not be attributed unambiguously by the $J_{1',2'}$ coupling constant and the $[\alpha]_D$ value. To clarify this point, the syrupy product **8** was fully deprotected in saturated methanolic HCl solution and then acetylated with acetic anhydride and pyridine. Recrystallization of the product gave white needles that were confirmed to be 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1-propene (**4**) by melting point, specific rotation, and also ^{1}H and ^{13}C NMR spectra. The α-anomeric configuration of **8** was thus clearly demonstrated by its chemical transformation into the known propene derivative **4**. The coupling constants of $J_{1',2'}$ 3.8 Hz, $J_{2',3'}$ 6.0 Hz, $J_{3',4'}$ 5.8 Hz, and $J_{4',5'}$ 4.6 Hz suggest [1c] that compound **8** exists as a conformational mixture [11] in rapid equilibrium between the $^4C_1$ and $^1C_4$ chair conformers, with significant population of the latter, having all substituents axial except that at C-1.

Protection at the 2-position as a phthalimido group is a well established procedure with 2-amino-2-deoxy sugars for the introduction of a 1,2-*trans*-glycosidic linkage. The influence of this protecting group on the anomeric stereoselectivity in the free-radical allylation reaction was here investigated. The reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide [16] with allyltributyltin (2 mol equiv) and AIBN (0.3 mol equiv) in dry toluene for 24 h at 85 °C under argon gave 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene (**9**) in 40% yield. The observed β-stereospecificity was expected as a consequence of the bulky and strongly participating 2-substituent. This large blocking group at C-2 decreased the rate of the free-radical reaction, and two portions of AIBN (0.15 mol equiv) were added to the solution. Purification on a column of silica gel provided **9** as a white solid, which could be crystallized from 3:1 hexanes–ethyl acetate to afford very beautiful needle crystals, mp 79–81 °C, $[\alpha]_D$ +70° in chloroform. ^{1}H NMR spectra of the initial fractions from

the column showed exclusively the β anomer. The ^{1}H NMR spectrum of the needle crystals showed that the β-allyl *C*-glycosyl derivative **9** co-crystallized with the solvents ethyl acetate and hexanes in the ratio of 1:0.25:0.2. The solvents could not be removed under vacuum at room temperature, and the crystals were very stable in air. Even on drying under diminished pressure at room temperature for 5 days, the ratio of **9** to solvents did not change. Eventually, the solvents were removed at 50 °C under vacuum to leave a glassy solid, which was demonstrated to be pure **9** by its ^{1}H NMR spectrum and elemental analyses.

A 1,2-elimination process was the major side-reaction in the preparation of **9**, and led to the glycal **10** in 16% yield. Because the elimination reaction generated hydrogen bromide in the system, the acetylated 2-deoxy-2-phthalimido-D-glucopyranosyl radical could also abstract a hydrogen radical from HBr, leading to the anhydro alditol **11**, formed in 8% yield. The glycal **10** and the alditol **11** had very similar R_f values. Recrystallization gave the pure white crystalline **10**, having mp 126–127 °C and $[\alpha]_D$ −11° in chloroform. Ogawa et al. [17] reported **10** as a syrup and $[\alpha]_D$ −15°. A pure preparation of **11** could not be obtained.

The β-anomeric configuration of **9** was assigned on the basis of ^{1}H NMR data for H-2′, which resonated as a triplet at δ 4.45 and showed $J_{1',2'}$ 10.1 Hz. The large values of $J_{2',3'}$, $J_{3',4'}$ and $J_{4',5'}$ (9.9, 9.3, and 10 Hz) were in accordance with the $^4C_1$ D-glycopyranosyl chair conformation. The β-*C*-glycosylpropene **9** showed an abnormally high dextrorotation ($[\alpha]_D$ +70° in chloroform). Such rotatory anomalies are known [18] in glycosides having certain aryl groups at C-2.

Although the acetylated 2-acetamido-2-deoxy-α-D-glucopyranosyl chloride (**1**) reacted with allyltributyltin in the presence of AIBN to produce the allylated product **4** in 67% yield, 3,4,5-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl chloride [19], in contrast to the bromide analogue, did not give any allylation product under the same free-radical allylation conditions. It appears that effective formation of an intermediate glycosyl radical requires a suitable combination of both the anomeric substituent and also the substituent group at C-2.

It is evident that both the anomeric substituent and the C-2 substituent play a major role in determining the course and stereoselectivity of the free-radical allylation reaction of 2-amino-2-deoxy-D-glucopyranosyl derivatives with allyltributyltin. 2-Amino-2-deoxy-D-glucopyranosyl derivatives having acetyl, trifluoroacetyl, and *p*-methoxybenzylidene protecting groups on the amino function favored formation of α-allylation products during the free-radical reaction. The α:β stereoselectivity for the *N*-acetyl protecting group was 34:1, and 11:1 for the *N*-trifluoroacetyl derivative; the *N*-*p*-methoxybenzylidene derivative gave exclusively the α product. The 2-phthalimido-2-deoxy-D-glucopyranosyl derivative gave exclusively the β-allylation product. The final steric outcome was not influenced by the configuration of the anomeric substituent. For 2-acetamido-2-deoxy-D-glucopyranosyl derivatives, both the α-substituted chloride **1** and the β-substituted xanthate derivative **2** gave preponderantly the α-allylation products. The nature of the anomeric substituent influenced the rate of the free-radical reaction. It took only 6 h for 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide to react completely, whereas the chloride derivative **1** required 8 h, and the xanthate derivative **2** required overnight reaction. The N-2 protecting group also influenced the rate of reaction. For 3,4,5-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide, it was necessary to add AIBN twice, and it took 24 h for all of the starting material to be consumed.

The stereoselectivity in reactions of glycosyl radicals can be expected to be controlled by both electronic and steric effects. According to the ESR studies of Giese [20], D-glycopyranosyl radicals may exist partially in the $B_{2,5}$ boat conformation and partially in the $^4C_1$ chair conformation of their precursors. Glycosyl radicals are fundamentally *p*-radicals and the unpaired electron occupies an orbital that has mainly *p*-character. The stereoelectronic effect makes attack from the α-face to the glycosyl radical in the $^4C_1$ chair conformation more favorable, because interaction is maintained in the transition state between the unpaired electron in the radical and the lone-pair electrons on the ring oxygen atom, and the α-product is obtained exclusively. The stereoselectivity is relatively low for glycosyl radicals in the $B_{2,5}$ boat conformation, even though α-attack is favored on stereoelectronic grounds. β-Attack is more favored for a glycosyl radical in the $^{1,4}B$ boat conformation. There is only a small energy difference between the $B_{2,5}$ boat and the $^{1,4}B$ boat, and this would account for the observed stereoselectivity [20].

Direct ESR investigation of 2-amino-2-deoxy-D-glucopyranosyl radicals was not pursued. Based on Giese's results, it was concluded that the acetylated 2-deoxy-2-*p*-methoxybenzylideneamino-D-glucopyranosyl radical should adopt the $^4C_1$ chair conformation, because of the steric strain caused by the large protecting group, and lead exclusively to the α-allylation product. The acetylated 2-acetamido-2-deoxy-D-glucopyranosyl and 2-trifluoroacetamido-2-deoxy-D-glucopyranosyl radicals should exist in the $B_{2,5}$ boat conformation and lead to an α,β mixture of products, with the α-product being preponderant. It is considered that the acetylated 2-phthalimido-2-deoxy-D-glucopyranosyl radical adopts the $^4C_1$ chair conformation, and the observed complete β-selectivity is attributable mainly to the steric effect. α-Attack is totally impeded by the rigid 2-phthalimido protecting group and the β-allylation product is formed exclusively.

The foregoing results show that the allyl group can be successfully introduced at the anomeric center of 2-amino-2-deoxy-D-glucopyranose derivatives through a free-radical reaction using allyltributyltin, with reasonable yields and short steps. The generality of this methodology was further evaluated with 2-amino-2-deoxy-D-galactopyranose and 2-amino-2-deoxy-D-mannopyranose.

Treatment of 2-acetamido-2-deoxy-D-galactose with acetyl chloride by the procedure [10] that converts the *gluco* analogue exclusively into the acetylated glycosyl chloride leads to 2-acetamido-3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl chloride in admixture with a smaller proportion of an oxazoline cyclization product **13**. This mixture was used directly in reaction with allyltributyltin and AIBN in dry toluene for 7 h at 85 °C under argon to afford 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-1-propene (**12**) in 56% yield (based on the glycosyl chloride precursor). The oxazoline **13**, which had an R_f value very close to that of the product **12**, was readily removed during the isolation procedure through hydrolysis in acidified acetone to a water-soluble product. Compound **12** was crystallized from 2:1 hexanes–ethyl acetate as needles, mp 129–130 °C; $[\alpha]_D$ +81° in chloroform. The α-anomeric configuration of **12** was confirmed by the $J_{1',2'}$ coupling constant of 4.8 Hz. The coupling constants between protons in the ring ($J_{1',2'}$ 4.8 Hz, $J_{2',3'}$ 9.4 Hz, and $J_{3',4'}=J_{4',5'}$ 3.2 Hz) indicate that **12** adopts the $^4C_1$ conformation in solution.

The reaction of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranosyl chloride (prepared from 2-acetamido-2-deoxy-D-mannose by the general procedure [10]) with allyltributyltin (3 mol equiv) and AIBN (0.15 mol equiv) in dry toluene did not give the desired allylation product, and instead the known [21] oxazoline **14** was obtained in 82% yield, mp 127–128 °C (from ether), $[\alpha]_D$ −31° in chloroform. Evidently the axial 2-acetamido group exerts a stronger neighboring-group participation effect than the equatorial group in the *gluco* and *galacto* series. The 1,2-ring-closure reaction is consequently much faster than the free-radical reaction, and so only the neighboring-group participating product, oxazoline **14**, is formed.

In conclusion, a carbon–carbon bond has been successfully introduced with high stereoselectivity at the anomeric center of activated 2-amino-2-deoxy-D-glycopyranosyl derivatives via a free-radical process. The stereoselectivity is controlled by the substituents at C-2. The acetyl, trifluoroacetyl and *p*-methoxybenzylidene protecting groups on the 2-amino function afford α-allylation products, whereas the phthalimido function provides a β-allylation product. The stereoselectivity is not influenced by the configuration of the substituent at the anomeric center. The rate of the free-radical reaction is controlled by the nature of the 2-substituent and the substituent at the anomeric center. The α-*C*-allylated glucopyranosyl compounds in solution have [1c] an appreciable proportion of the $^1C_4$ conformers in equilibrium with the $^4C_1$ conformers.

3. Experimental

General methods.—Evaporations were conducted under diminished pressure. Reaction solvents were purified and dried by distillation as recommended. TLC was performed on precoated plates of Silica Gel 60F-254 (E. Merck); components were detected by UV light and by spraying the plates with 10% H_2SO_4 and subsequent heating. Flash-column chromatography was performed on 230–240 mesh silica gel (E. Merck). Melting points were determined in open glass capillaries in a Thomas–Hoover apparatus, and are uncorrected. Specific rotations were determined with a Perkin–Elmer Model 241MC polarimeter at 20 °C, unless otherwise noted. ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker AM-250 (250 MHz ^{1}H,

62.5 MHz ^{13}C), AM-300 (300 MHz ^{1}H, 75.5 MHz ^{13}C), and AM-500 (500 MHz ^{1}H, 125 MHz ^{13}C) spectrometers. Chemical shifts (ppm) are relative to Me_4Si as the internal standard. Splitting patterns are designated: s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet. Spectra with the AM-500 instrument at The Ohio State University Instrument Center were recorded by Dr. C. E. Cottrell. All signal assignments were verified by ^{1}H–^{1}H and ^{13}C–^{1}H correlation spectra. Fast-atom-bombardment (FAB) mass spectra were recorded at The Ohio State University Instrument Center with Kratos VG 70-250S mass spectrometers by D. Chang. Elemental analyses were performed by Atlantic Microlabs, Atlanta, Georgia.

General procedure for free-radical allylation of activated 2-amino-2-deoxy sugars.—A suspension or solution of the activated 2-amino-2-deoxy sugar derivative (1 mol equiv), allyltributyltin (2–3 mol equiv), and AIBN (0.15 mol equiv) in dry toluene was degassed for 10 min and the mixture was then stirred at 85 °C under Ar. A clear solution was obtained during the first hour of heating. After the starting material had been consumed completely, the toluene solvent was evaporated off and the residue was dissolved in MeCN. The solution was washed three times with pentane and evaporated. The residue was purified on a column of silica gel to provide the pure allylation product.

*3-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucopyranosyl)-1-propene* (**4**).—*(a) From 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucopyranosyl chloride* (**1**). The general free-radical allylation procedure was followed. A suspension of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride [10] (**1**, 10.97 g, 30 mmol), allyltributyltin (29 mL, 91 mmol) and AIBN (738 mg, 4.5 mmol) in dry toluene (60 mL) was degassed for 10 min, and the mixture was then stirred at 85 °C under Ar for 8 h. TLC showed the complete absence of starting material (R_f 0.64, EtOAc) and the presence of three new spots having R_f 0.49, 0.46, and 0.08 (EtOAc). The crude products were chromatographed on a column of silica gel, eluting with 4:1 EtOAc–hexanes to give the product **4** as a white solid (7.46 g, 67%). This solid was crystallized from 1:3 EtOAc–hexanes, and further recrystallization afforded the pure product **4** as needles having mp 109–110 °C; $[\alpha]_D$ +47° (*c* 1.2, $CHCl_3$); R_f 0.49 (EtOAc); NMR data see Tables 1–3; MS: *m/z* 372 $(M+H)^+$, 330 $(M-allyl)^+$, 312 $(M+H-HOAc)^+$, 270 $(M-HOAc-allyl)^+$. Anal. Calcd for $C_{17}H_{25}NO_8$ (371.383): C, 54.98; H, 6.79; N, 3.77. Found: C, 54.82; H, 6.85; N, 3.73.

Evaporation of the mother liquor from the recrystallization gave a syrup, which was demonstrated by its ^{1}H NMR spectrum to be a mixture of **4** and its β anomer. A total of 0.22 g of the β anomer of **4** was present (NMR integration) in the mother liquor (2% yield), which had the same R_f value as **4**. It was not found possible to obtain the β anomer of **4** pure through chromatography and recrystallization. ^{1}H NMR data for the β anomer of **4** (300 MHz, C_6D_6): δ 5.93 (tdd, 1 H, $J_{1a,2}$ 10.3 Hz, $J_{1b,2}$ 17.1 Hz, $J_{2,3a} = J_{2,3b}$ 6.9 Hz, H-2), 5.24 (dd, 1 H, $J_{3',4'}$ 9.4 Hz, $J_{4',5'}$ 9.8 Hz, H-4'), 5.19 (d, 1 H,

Table 1
^{1}H NMR chemical shifts (δ) and multiplicities of 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1-propene[a] (**4**), 3-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl)-1-propene hydrochloride[b] (**7**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl)-1-propene[c] (**8**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene[a] (**9**) and 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-1-propene[a] (**12**)

Compound	H-1a	H-1b	H-2	H-3a	H-3b	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′a	H-6′b	N-H	Ac
4	4.98 dq	5.00 dq	5.68 tdd	2.27 ddd	2.07 ddd	4.21 ddd	4.52 ddd	5.19 dd	5.08 t	3.88 ddd	4.35 dd	4.11 dd	5.80 d	1.70,1.62 1.60,1.58
7	5.14 dq	5.20 dq	5.76 tdd	2.61 m	2.61 m	4.44 ddd	3.79 dd	5.40 dd	4.95 dd	3.89 ddd	4.26 dd	4.06 dd	8.66 bs	2.16,2.08 2.06
8	4.96 dq	4.99 dq	5.61 tdd	2.25 ddd	2.03 ddd	4.08 ddd	4.30 ddd	5.12 dd	4.93 dd	3.93 ddd	4.43 dd	4.02 dd	7.07 d	1.69,1.59 1.57
													Phth	
9	4.81 dq	4.84 dq	5.73 tdd	2.17 m	2.17 m	4.53 ddd	4.44 t	6.08 dd	5.31 dd	3.41 ddd	4.26 dd	4.01 dd	7.46 6.86	1.70,1.63 1.46
12	4.98 dq	5.00 dq	5.67 tdd	2.19 m	2.00 m	4.37 m	4.76 ddd	5.16 dd	5.40 t	3.94 m	4.36 dd	4.21 dd	5.44 d	1.67,1.66 1.63,1.50

[a]At 300 MHz in C_6D_6.
[b]At 300 MHz in $CDCl_3$.
[c]At 500 MHz in C_6D_6.

Table 2
The first-order ^1H–^1H coupling constants (Hz) of 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1-propene[a] (**4**), 3-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl)-1-propene hydrochloride[b] (**7**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl)-1-propene[c] (**8**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene[a] (**9**) and 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-1-propene[a] (**12**)

Compound	$J_{1a,2}$	$J_{1b,2}$	$J_{1a,3a}$	$J_{1b,3a}$	$J_{1a,3b}$	$J_{1b,3b}$	$J_{2,3a}$	$J_{2,3b}$	$J_{3a,3b}$	$J_{3a,1'}$	$J_{3b,1'}$
4	10.2	17.0	~1	~1	~1	~1	6.8	6.8	11.5	10.0	4.8
7	10.3	17.4	~1	~1	~1	~1		6.4	6.4	10.5	4.9
8	10.2	17.1	~1	~1	~1	~1	6.9	6.9	14.5	9.0	5.3
9	10.2	17.1	~1	~1	~1	~1	6.9	6.9		5.2	5.2
12	10.2	17.0	~1	~1	~1	~1	6.8	6.8			

Compound	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$	$J_{NH,2'}$
4	4.5	8.2	6.8	6.8	6.5	3.8	11.9	8.7
7	4.8	8.8	7.9	8.0	6.0	3.0	12.2	
8	3.8	6.0	5.8	4.6	7.3	4.5	11.9	9.2
9	10.2	10.2	9.0	10.3	4.5	2.1	12.3	
12	4.8	9.4	3.2	3.2	7.1	5.4	11.5	8.4

[a]At 300 MHz in C_6D_6.
[b]At 300 MHz in $CDCl_3$.
[c]At 500 MHz in C_6D_6.

Table 3
^{13}C NMR chemical shifts (δ) of 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1-propene[a] (**4**), 3-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl)-1-propene hydrochloride[b] (**7**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl)-1-propene[c] (**8**), 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene[c] (**9**) and 3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-1-propene[d] (**12**)

Compound	C-1	C-2	C-3	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′		
4	117.56	133.26	32.05	70.86	50.47	70.01	67.85	70.58	61.58		
7	118.67	133.93	32.91	70.42	51.78	69.65	68.96	72.25	62.23		
8	118.00	133.20	33.71	69.22	50.02	68.87	67.36	72.45	60.88		
9	117.67	133.12	36.94	74.73	55.21	72.38	69.47	76.22	62.28		
12	117.38	133.42	31.38	71.09	48.74	68.16	66.80	68.77	61.25		
Compound	$COCH_3$	$COCH_3$	$COCH_3$	$COCH_3$	$COCF_3$	C=O	C=O	C=O	C=O	Phth	Phth
4	23.10	20.74	20.64	20.64		170.86	170.55	169.59	168.92		
7	20.78	20.64	20.64			172.22	171.18	171.01			
8	20.20	19.98	19.98		116.52	170.10	169.84	168.53	156.91		
9	20.31	20.15	19.93			170.00	169.16	168.00	167.58	134.13	134.00
										134.07	133.90
										123.63	123.27
12	23.02	20.71	20.58	20.53		170.61	170.44	169.99	169.90		

[a]At 63 MHz in $CDCl_3$.
[b]At 75 MHz in CD_3OD.
[c]At 75 MHz in C_6D_6.
[d]At 75 MHz in $CDCl_3$.

$J_{NH,2'}$ 10.5 Hz, N-H), 5.12 (dd, 1 H, $J_{2',3'}$ 9.2 Hz, H-3′), 5.09 (d, 1 H, H-1a), 5.06 (d, 1 H, H-1b), 4.34 (dd, 1 H, $J_{5',6'a}$ 4.9 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.16 (m, 2 H, H-2′ and H-6′b), 3.51 (ddd, 1 H, $J_{5',6'b}$ 2.3 Hz, H-5′), 3.16 (ddd, 1 H, $J_{1',2'}$ 10.1 Hz, $J_{1',3a}$ 3.8 Hz, $J_{1',3b}$ 7.4 Hz, H-1′), 2.32 (m, 2 H, H-3a and H-3b), 1.74, 1.73, 1.71, and 1.63 (4s, 4×3H, 4-$COCH_3$).

Preparation of an inseparable 10:1 mixture of **4** and its β anomer as a waxy solid has been reported [9j].

The side-product, 4,5-dihydro-2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyranoso)-[2,1-*d*]-1,3-oxazole (**5**, R_f 0.46, EtOAc) was obtained as a syrup (0.49 g, 5%), $[\alpha]_D$ +13° (*c* 1.3, $CHCl_3$); lit. [22]. syrup, $[\alpha]_D$ +12° (*c* 1.0, $CHCl_3$). The fraction having R_f 0.08 (EtOAc) was evaporated to a white solid, which was demonstrated by its mass spectrum to be an oligomeric mixture (2.69 g, 24%), MS: *m/z* 1114 $(3M+H)^+$, 743 $(2M+H)^+$ (M: molecular mass of compound **4**).

*(b) From 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl ethylxanthate* (**2**). The general free-radical allylation procedure was followed. A suspension of 2-acetamido-3,4,6-tri-*O*-acetyl-2-

deoxy-β-D-glucopyranosyl ethylxanthate [12] (**2**, 903 mg, 2 mmol), allyltributyltin (1.24 mL, 4 mmol), and AIBN (49.3 mg, 0.3 mmol) in dry toluene (4 mL) was degassed for 10 min. The mixture was stirred for 24 h at 80 °C under Ar. The crude products were chromatographed on a column of silica gel (4:1 EtOAc–hexanes) to give **4** as a white solid (184 mg, 25%).

(c) Attempted preparation from 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl bromide (**3**). The general free-radical allylation procedure was followed. To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide [13] (**3**, 1.04 g, 2.52 mmol) and AIBN (62.1 mg, 0.38 mmol) in dry toluene (4 mL) and 1,2-dimethoxyethane (DME, 2 mL) was added allyltributyltin (1.56 mL, 4.88 mmol). The solution was degassed for 10 min and then heated for 18 h at 80 °C under Ar. TLC (EtOAc) showed a single spot (R_f 0.44) for the oxazoline **5**. The crude product was purified on a short column of silica gel, eluting with EtOAc to afford compound **5** as a syrup (735.6 mg, 88%).

3-(2-Acetamido-2-deoxy-α-D-glucopyranosyl)-1-propene (**6**).—A solution of compound **4** (1.11 g, 3 mmol) in dry MeOH (15 mL) was treated with 25 wt% of NaOMe in MeOH (0.03 mL) for 10 min at room temperature, and then made neutral with Amberlite IR-120 (H^+) resin. The resin was filtered off, washed with MeOH, and the filtrate was evaporated to afford a white solid (0.73 g, 100%), which was recrystallized from EtOH to afford white crystalline **6**: mp 204–206 °C; $[\alpha]_D$ +109° (*c* 1.0, MeOH); R_f 0.38 (2:1 EtOAc–EtOH); ^{1}H NMR (300 MHz, CD_3SOCD_3): δ 7.70 (d, 1 H, $J_{2',NH}$ 7.6 Hz, NHAc), 5.75 (tdd, 1 H, $J_{1a,2}$ 10.2 Hz, $J_{1b,2}$ 17.1 Hz, $J_{2,3a} = J_{2,3b}$ 6.9 Hz, H-2), 5.05 (bd, 1 H, H-1b), 4.97 (dd, $J_{1b,3}$~1.0 Hz, H-1a), 4.89 (d, 1 H, $J_{4',OH}$ 4.1 Hz, O*H*-4'), 4.75 (bs, 1 H, O*H*-3'), 4.35 (t, 1 H, $J_{6'a,OH} = J_{6'b,OH}$ 5.9 Hz, O*H*-6'), 3.86 (td, 1 H, $J_{1',2'} = J_{1',3b}$ 4.8 Hz, $J_{1',3a}$ 10.0 Hz, H-1'), 3.69 (m, 1 H, $J_{2',3'}$ 10.9 Hz, H-2'), 3.56 (ddd, 1 H, $J_{5',6'a}$ 2.5 Hz, $J_{6'a,6'b}$ 11.5 Hz, H-6'a), 3.44 (m, 2 H, H-3', H-6'b), 3.27 (m, 1 H, H-5'), 3.13 (m, 1 H, H-4'), 2.33 (m, 1 H, H-3a), 2.11 (m, 1 H, H-3b), 1.81 (s, 3 H, NHCO CH_3); ^{13}C NMR (75 MHz, CD_3SOCD_3): δ 169.16 ($NHCOCH_3$),135.56 (C-2), 116.23 (C-1), 73.81 (C-5'), 72.36 (C-1'), 71.00 (C-3'), 70.37 (C-4'), 61.03 (C-6'), 53.11 (C-2'), 30.19 (C-3), 22.64 ($NHCOCH_3$); MS: *m/z* 268 $(M+Na)^+$, 246 $(M+H)^+$, 204 $(M-allyl)^+$. Anal. Calcd for $C_{11}H_{19}NO_5$ (245.273): C, 53.87; H, 7.81; N, 5.71. Found: C, 53.89; H, 7.76; N, 5.64.

3-(3,4,6-Tri-O-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl)-1-propene hydrochloride (**7**).—The general free-radical allylation procedure was followed. A solution of 3,4,6-tri-*O*-acetyl-2-*p*-methoxybenzylideneamino-2-deoxy-α-D-glucopyranosyl bromide [14] (928 mg, 1.91 mmol), allyltributyltin (1.80 mL, 5.8 mmol), and AIBN (66.1 mg, 0.4 mmol) in dry toluene (6 mL) was degassed for 10 min. The mixture was heated for 9 h at 90 °C under Ar and then cooled to room temperature. To the solution was added additional AIBN (62 mg, 0.37 mmol). The solution was degassed for another 10 min and heated at 80 °C overnight again under Ar. The crude products were dissolved in Et_3N (0.5 mL) and EtOAc (0.5 mL), and purified on a column of silica gel with 1:1 EtOAc–hexanes to give a light-yellow syrupy product: 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-*p*-methoxybenzylideneamino-α-D-glucopyranosyl)-1-propene (387 mg, 45%). This syrup was dissolved in acetone (4 mL) and to the solution were added 4 drops of 6 M HCl. A white precipitate formed immediately that was identified as compound **7**: mp 220–222 °C (dec); $[\alpha]_D$ +59° (*c* 0.53, MeOH); NMR data see Tables 1–3; MS: *m/z* 330 $(M-Cl)^+$, 288 $(M-HCl-allyl)^+$, 270 $(M-HCl-OAc)^+$. Anal. Calcd for $C_{15}H_{24}ClNO_7$ (365.807): N, 3.83. Found: N, 4.24.

Compound **7** was suspended in CH_2Cl_2 and then washed with satd. $NaHCO_3$ and brine, and dried over Na_2SO_4. After filtration and evaporation, compound **7a** was obtained as a syrup; NMR data (1 H, 300 MHz, $CDCl_3$): δ 5.81 (tdd, 1 H, $J_{1a,2}$ 10.1, $J_{1b,2}$ 16.9, $J_{2,3a} = J_{2,3b}$ 7.0 Hz, H-2), 5.16 (dq, 1 H, $J_{1b,3}$ 1, $J_{1a,1b}$ 1 Hz, H-1b), 5.13 (dq, 1 H, $J_{1a,3}$ 1 Hz, H-1a), 5.05 (dd, 1 H, $J_{2',3'}$ 9.4, $J_{3',4'}$ 8.8 Hz, H-3'), 4.89 (t, 1 H, $J_{4',5'}$ 8.8 Hz, H-4'), 4.24 (dd, 1 H, $J_{5',6'a}$, 5.7, $J_{6'a,6'b}$ 12.0 Hz, H-6'a), 4.08 (m, 1 H, H-1'), 4.06 (dd, 1 H, $J_{5',6'b}$ 2.7 Hz, H-6'b), 3.86 (ddd, 1 H, H-5'), 3.14 (dd, 1 H, $J_{1',2'}$ 5.3 Hz, H-2'), 2.47 (m, 2 H, H-3a,3b), 2.09, 2.07, and 2.04 (3s, 3×3 H, 3 OAc), 1.30 (bs, 2 H, NH2).

3-(3,4,6-Tri-O-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl)-1-propene (**8**).—The general free-radical allylation procedure was followed. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide [15] (931.4 mg, 2 mmol), allyltributyltin (1.24 mL, 4 mmol), and AIBN (57.8 mg, 0.35 mmol) in dry toluene (6 mL) was degassed for 15 min, and the mixture was then heated for 6 h at 80–85 °C under Ar. The crude products were purified on a column of silica gel that was eluted with 1:2 EtOAc–hexanes to afford

a mixture of the α and β anomers of **8** as a colorless syrup (559.4 mg, 65%, $\alpha:\beta = 12:1$). The mixture was dissolved in hot 1:4 EtOAc–hexanes, and then a syrup that separated was collected, which was pure **8**: $[\alpha]_D$ +22° (*c* 1.1, $CHCl_3$); R_f 0.52 (1:1 EtOAc–hexanes); NMR data see Tables 1–3; MS: *m/z* 426 $(M+H)^+$, 384 $(M-allyl)^+$, 366 $(M-OAc)^+$, 324 $(M\text{-}HOAc-allyl)^+$, 306 $(M+H-2HOAc)^+$, 264 $(M-2HOAc-allyl)^+$. Anal. Calcd for $C_{17}H_{22}F_3NO_8$ (425.354): C, 48.00; H, 5.21; N, 3.29. Found: C, 48.10; H, 5.18; N, 3.30.

Conversion of compound **8** *into its 2-acetamido analogue* **4**.—A solution of **8** in satd methanolic HCl was stirred at room temperature until TLC showed complete disappearance of **8**, whereupon the soln was evaporated. The residue was dissolved in pyridine and treated with an excess of Ac_2O. The solution was kept overnight and then poured into ice-water. Conventional processing gave compound **4** as needles identical with authentic **4** by mp, $[\alpha]_D$, and ^1H and ^{13}C NMR spectra.

*3-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl)-1-propene* (**9**).—*(a) From 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl bromide*. The general free-radical allylation procedure was followed. To a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl bromide [16] (1.49 g, 3 mmol) and AIBN (73.9 mg, 0.45 mmol) in dry toluene (6 mL) was added allyltributyltin (1.86 mL, 6 mmol). The solution was degassed for 15 min, then heated for 20 h at 85 °C under Ar, and then cooled to room temperature. A second portion of AIBN (74.8 mg, 0.45 mmol) was added to the solution, which was again degassed for 15 min and heated for 4 h under Ar at 90 °C. TLC showed the complete disappearance of the strongly charring spot at R_f 0.47 (1:1 EtOAc–hexanes) for the starting material. The product **9** had the same R_f value as the starting material, but showed a very light color after spraying with 10% sulfuric acid and subsequent heating, and another new spot at R_f 0.29 was present. The crude products were purified on a column of silica gel, eluting with 1:1 EtOAc–hexanes, to give compound **9** as a white solid (543.1 mg, 40%), which crystallized from 1:3 EtOAc–hexanes to provide white crystals; mp 79–81 °C; $[\alpha]_D$ +70° (*c* 1.2, $CHCl_3$); The ^1H NMR spectrum showed that the white crystalline product was a solvate with EtOAc and hexanes in the ratio of 1:0.25:0.20, which was very stable in air. The solvating solvents were removed at 50 °C under vacuum to afford a pure glassy product **9**. NMR data see Tables 1–3; MS: *m/z* 460 $(M+H)^+$, 418 $(M\text{-allyl})^+$, 400 $(M-OAc)^+$, 358 $(M-HOAc-allyl)^+$, 340 $(M+H-2HOAc)^+$, 298 $(M-2HOAc-allyl)^+$, 280 $(M+H-3HOAc)^+$. Anal. Calcd for $C_{23}H_{25}NO_9$ (459.448): C, 60.13; H, 5.48; N, 3.05. Found: C, 60.02; H, 5.56; N, 3.10.

A nonsolvated form of **9** has been reported [9j] to have mp 105–106 °C.

The second fraction (R_f 0.29, 1:1 EtOAc–hexanes) was evaporated to a syrup, whose ^1H NMR spectrum indicated it to be a mixture of the glycal elimination product **10** (16%) and a reduction product, 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-phthalimido-D-glucitol (**11**) (8%). After recrystallization from 1:4 EtOAc–hexanes, 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-phthalimido-D-*arabino*-hex-1-enitol (**10**) was obtained as colorless needles: mp 126–127 °C; $[\alpha]_D$ −11° (*c* 0.57, $CHCl_3$); lit [17]. syrup, $[\alpha]_D$ −15° (*c* 0.20, $CHCl_3$); ^1H NMR data for compound **10** (300 MHz, C_6D_6): δ 7.44 and 6.83 (m, 4 H, Phth), 6.44 (s, 1 H, H-1), 5.95 (d, 1 H, $J_{3,4}$ 4.0 Hz, H-3), 5.36 (dd, 1 H, $J_{4,5}$ 4.7 Hz, H-4), 4.48 (dd, 1 H, $J_{5,6a}$ 6.4 Hz, $J_{6a,6b}$ 11.8 Hz, H-6a), 4.27 (m, 1 H, H-5), 4.20 (dd, 1 H, $J_{5,6b}$ 3.8 Hz, H-6b), 1.65, 1.62, 1.47 (3s, 3×3 H, 3OAc); ^1H NMR data for **11** (300 MHz, C_6D_6): δ 7.43 and 6.87 (m, 4 H, Phth), 6.06 (dd, 1 H, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 9.1 Hz, H-3), 5.28 (dd, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 4.63 (ddd, 1 H, $J_{1a,2}$ 11.4 Hz, $J_{1e,2}$ 5.5 Hz, H-2), 4.26 (t, 1 H, $J_{1a,1e}$ 11.2 Hz, H-1a), 4.25 (dd, 1 H, $J_{5,6a}$ 4.6 Hz, $J_{6a,6b}$ 12.3 Hz, H-6a), 4.05 (dd, 1 H, $J_{5,6b}$ 2.1 Hz, H-6b), 3.56 (dd, 1 H, H-1e), 3.35 (ddd, 1 H, H-5), 1.70, 1.61, and 1.44 (3s, 3OAc).

(b) Attempted C*-allylation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl chloride*. The same reaction conditions as used for the free-radical reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl bromide with allyltributytin initiated with AIBN in toluene solvent were used with 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl chloride [19]. However, no compound **9** was detected in the product mixture.

*3-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*α*-*D*-galactopyranosyl)-1-propene* (**12**).—The general free-radical allylation procedure was followed. To a soln of a mixture of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*α*-D-galactopyranosyl chloride and oxazoline **13** (1.2456 g, 1:0.85 by ^1H NMR spectrum, 1.93 mmol of the chloride derivative, prepared from 2-acetamido-2-deoxy-D-galactose by the general procedure [10]) in dry toluene (7 mL)

were added allyltributyltin (3.27 mL, 10.7 mmol) and AIBN (87.4 mg, 0.53 mmol). The soln was degassed for 10 min and then heated for 7 h at 85 °C under Ar. The crude products were chromatographed on a column of silica gel with 4:1 EtOAc–hexanes to afford a mixture of product **12** and oxazoline **13**. To a soln of the mixture in acetone (20 mL) was added a 1% aqueous soln of HCl (1 mL) to convert the oxazoline **13** into a more polar compound, 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranose hydrochloride, to facilitate separation. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2. The soln was washed successively with satd $NaHCO_3$, brine, dried (Na_2SO_4) and evaporated to a syrup, which was chromatographed on a column of silica gel with 4:1 EtOAc–hexanes to give **12** as a white solid (293.5 mg, 56%). The white solid was recrystallized from 1:2 EtOAc–hexanes to provide white crystals of **12**: mp 129–130 °C; $[\alpha]_D$ +81° (*c* 1.0, $CHCl_3$); R_f 0.39 (EtOAc); NMR data see Tables 1–3; MS: *m/z* 372 $(M+H)^+$, 330 $(M-allyl)^+$, 312 $(M-OAc)^+$, 270 $(M-HOAc-allyl)^+$, 252 $(M+H-2HOAc)^+$. Anal. Calcd for $C_{17}H_{25}NO_8$ (371.383): C, 54.98; H, 6.79; N, 3.77. Found: C, 54.90; H, 6.76; N, 3.75.

*4,5-Dihydro-2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-*β*-D-mannopyranoso)-[2,1-d]-1,3-oxazole* (**14**).—The general free-radical allylation procedure was followed. To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranosyl chloride (prepared from 2-acetamido-2-deoxy-D-mannose by the general procedure [10]) (620.7 mg, 1.7 mmol) and AIBN (41.8 mg, 0.25 mmol) in dry toluene (4 mL) was added allyltributyltin (1.63 mL, 5.1 mmol). The solution was degassed for 15 min and then heated for 6 h at 85 °C under Ar. The crude products were applied to a short column of silica gel. Washing the column with EtOAc and evaporation of the eluate gave a crystalline residue of **14** (458.0 mg, 82%). Recrystallization from ether afforded needles of **14**: mp 127–128 °C; $[\alpha]_D$ −31° (*c* 1.0, $CHCl_3$); lit [22]. mp 132–133 °C; $[\alpha]_D$ −30° (*c* 1.0, $CHCl_3$).

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