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Synthesis of vinyl glycosides and carbohydrate vinyl ethers from mixed acetals: a hetero-Diels–Alder approach to deoxygenated disaccharides

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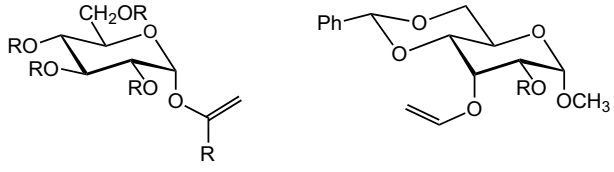
Abstract—A new method for the synthesis of vinyl glycosides and carbohydrate vinyl ethers is described. Mixed acetal glycosides and other types of carbohydrate mixed acetals are treated with TMS-triflate and an amine base, conditions developed by Gassman for the synthesis of enol ethers from acetals. The elimination proceeds regioselectively in most cases but also gives silyl ethers as side products in others. The hetero-Diels–Alder reactions of carbohydrate 3-*O*- and 6-*O*-vinyl ethers with ethyl (*E*)-ethoxymethylenepyruvate were carried out as part of a model study for the synthesis of deoxygenated disaccharides of antibiotics.

1. Introduction

Carbohydrates in which the anomeric hydroxyl group is derivatized as a vinyl ether (vinyl glycosides) have numerous applications in carbohydrate chemistry. Vinyl glycosides have been used as substrates in cycloaddition reactions, both as chiral auxiliaries in inverse-electron-demand cycloadditions to give homochiral tetralins,[1] and as precursors to enantiomerically pure cyclobutanols.[2] Vinyl glycosides that are unsaturated at C2–C3 undergo thermal Claisen rearrangement to give C-3 branched glycal derivatives.[3] Isopropenyl[4] and butenyl[5] glycosides have been used extensively as glycosyl donors in oligosaccharide synthesis. Structurally related carbohydrate vinyl ethers, in which the vinyl group is attached to nonanomeric hydroxyl groups, have been utilized in the synthesis of cyclooctanoic mimetics of carbohydrates,[6] as precursors to *C*-glycosides,[7] and as intermediates in the synthesis of β-mannosides by intramolecular tethering and delivery.[8] In studies of carbohydrate processing enzymes, vinyl glycosides and mixed acetal glycosides have been investigated as substrates for glycosidases.[9] Structures of vinyl glycosides and a carbohydrate vinyl ether are illustrated in Figure 1.



vinyl glycosides 3-*O*-vinyl ether

Figure 1. Vinyl glycosides and carbohydrates vinyl ethers.

These applications demonstrate the potential of vinyl glycosides and related carbohydrate vinyl ethers in synthetic carbohydrate chemistry; however, there are drawbacks associated with their preparation. The synthesis of these compounds is usually carried out with mercury reagents. Most other methods involve several steps and proceed in low overall yield. Vinyl glycosides are most often synthesized by transvinylation with mercuric acetate[10] or from glycosyl halides by nucleophilic displacement with bis(acylmethyl)mercury reagents.[11] Elimination reactions of 2-(phenylselenyl)ethyl glycosides[12] and 2-(trimethylammonium)ethyl glycosides,[10] and photolysis of 4-oxopentyl glycosides by Norrish type II reactions also give vinyl glycosides.[13] Palladium-catalyzed vinylation of protected monosaccharides has recently been reported,[14] and Tebbe methylenation has been used to prepared both vinyl glycosides and vinylated sugar derivatives involving a

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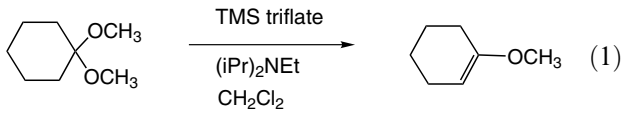
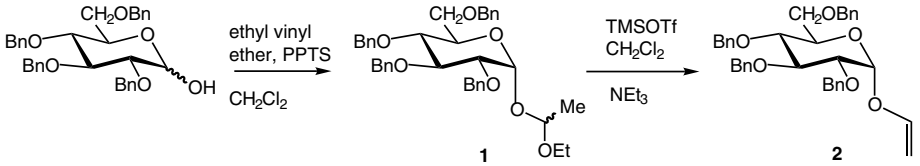
nonanomeric hydroxyl group.[4,7] In earlier studies, the addition of acetylene at high pressure was used to prepared vinyl ethers of carbohydrates for use in polymer synthesis.[15]



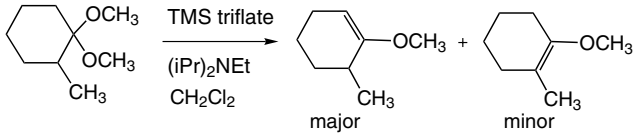
(1)

Our research on the synthesis of carbohydrate components of antibiotics required a flexible, efficient route to carbohydrate vinyl ethers, as part of a program aimed at oligosaccharides that contain highly deoxygenated sugars. In preliminary studies, we have demonstrated that a new route to vinyl glycosides and carbohydrate vinyl ethers can be developed based upon a synthesis of vinyl ethers from symmetrical acetals, first reported by Gassman in 1994.[16] In this reaction, acetals are treated with trimethylsilyltrifluoromethane sulfonate and DIPEA (Eq. 1). Dujardin et al. reported the preparation of vinyl ethers derived from chiral secondary alcohols such as menthol using a similar method, with triethylamine as the base.[17] The application of three methods to the synthesis of vinyl glycosides requires the preparation of mixed acetal glycosides, which are readily accessible by the treatment of monosaccharides with simple vinyl ethers in the presence of an acid catalyst.[18] The resulting mixed acetals are then subjected to the elimination reaction. In preliminary studies, we found that the mixed acetal glycoside derived from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside and ethyl vinyl ether underwent facile elimination in the presence of trimethylsilyltrifluoromethanesulfonate and triethylamine to give vinyl α-D-glucopyranoside **2** in 68% yield after purification by flash chromatography (Eq. 2).[19] Products resulting from ring-opening or glycals derived from elimination of the anomeric substituent were not observed. Herein, we describe the preparation of a number of vinyl glycosides and carbohydrate vinyl ethers using this method. Two examples of the use of carbohydrate vinyl ethers in hetero-Diels–Alder reactions are also described.



(2)

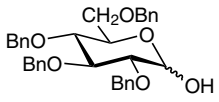
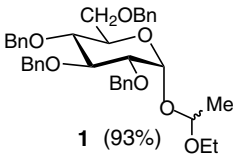
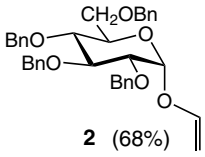
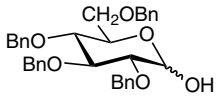
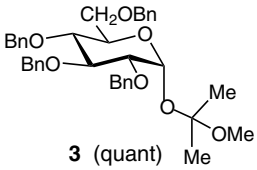
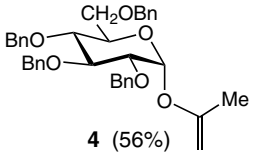
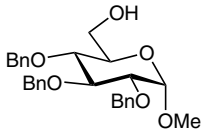
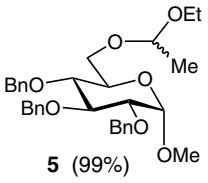
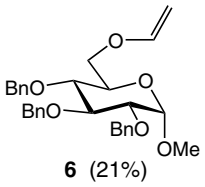
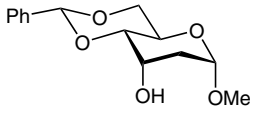
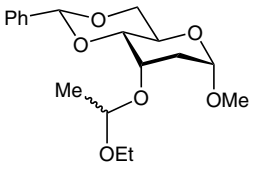
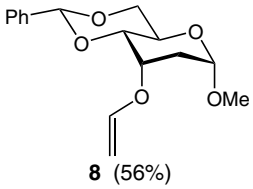
Vinyl glycosides and carbohydrate vinyl ethers that were prepared herein are shown in Table 1. Monosaccharides were treated with ethyl vinyl ether (entries 1, 3, and 4) or 2-methoxypropene (entry 2) in the presence of PPTS to give mixed acetals. Reactions were straightforward and conversions were usually complete within 2 h, with no side products observed. In reactions involving ethyl vinyl ether, a mixture of diastereomers is produced in nearly equal amounts, with no attempt at separation being made. However, extensive NMR assignments could be carried out on the mixture. For mixed acetal **1**, the ratio of α to β anomer was 9:1, while only traces of β anomer were observed for **3**. The elimination step could be carried out without any further purification of the mixed acetals; however, longer reaction times, up to two days in some cases, were required. Purification of the mixed acetals could be carried out by column chromatography on Florisil because the acid-sensitivity of these compounds precludes the use of silica gel. Treatment of the mixed acetal glycosides with TMS-triflate and triethylamine gave the desired vinylated products in acceptable yields, with the exception of the 6-*O*-vinyl ether. The main cause for reduction in yield of the vinylated product in the elimination step is the competing formation of silyl ether (Scheme 1). Complexation of the trimethylsilyl cation with the anomeric oxygen gives intermediate **A**, in which the O1 (pyranose)–CH bond is activated for cleavage, and results in formation of silyl ether **9**. Silyl ether **9** was isolated along with vinyl glycosides **2** and **4**. Complexation of the trimethylsilyl cation with the ethoxy group oxygen gives intermediate **B** and produces the desired vinyl glycosides. Competition between these two pathways ultimately determines the regioselectivity of the elimination step, and previous studies reveal some interesting characteristics of this type of process.

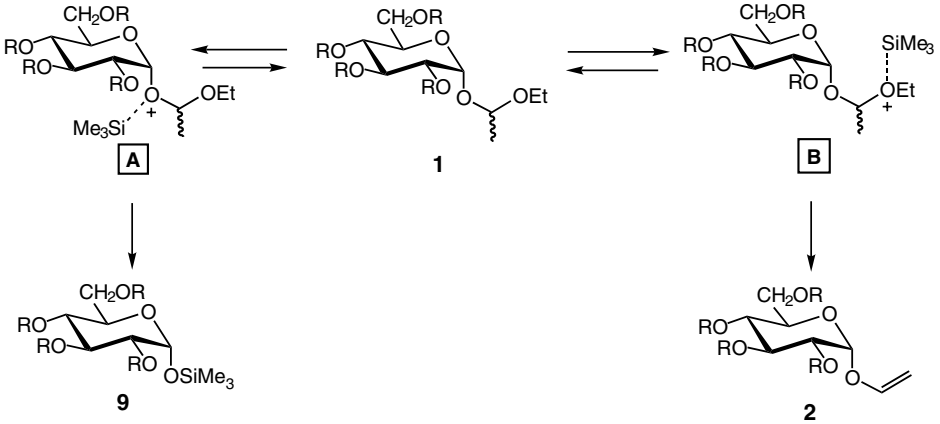


(3)

The results Gassman obtained with acetals derived from cyclic ketones revealed a preference for the formation of the less-substituted alkene from unsymmetrical substrates (Eq. 3), and it was proposed that this occurs in the elimination step by abstraction of the less hindered proton by the hindered base. The ratio of the major and minor products (88:12) does not correspond to the expected thermodynamic ratio (63:37) for the dimethyl acetal derived from 2-methylcyclohexanone, as the authors noted, yet the reaction was thought to proceed from an initial and reversible complexation of the silyl-

Table 1. Synthesis of vinyl glycosides and carbohydrate vinyl ethers

Entry	Substrate	Mixed acetal	Vinylated product
1		 **1** (93%)	 **2** (68%)
2		 **3** (quant)	 **4** (56%)
3		 **5** (99%)	 **6** (21%)
4		 **7** (92%)	 **8** (56%)

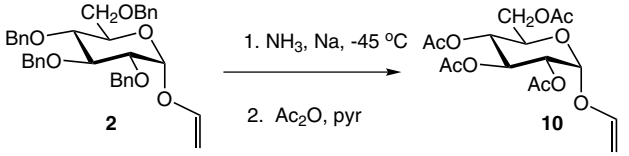


Scheme 1. Regioselectivity of vinyl glycoside formation.

ating reagent. Loss of a proton from the sterically less hindered site seems to provide the basis for selectivity according to these authors. The importance of steric factors in the elimination was further demonstrated in the study of Dujardin, in which different bases influenced the regioselectivity of the elimination from mixed acetals of menthol and other alcohols.[17] As applied to carbohydrate substrates in this study, the Gassman procedure gave acceptable yields of vinyl glycosides with minimal formation of silyl ether in entries 1 and 4 in Table 1. We had only modest success in obtaining less silyl ether in one case by using diisopropylethylamine instead of triethylamine (entry 2). A more extensive survey of reaction conditions needs to be conducted to optimize the elimination step for vinyl glycoside and carbohydrate vinyl ether synthesis. The silyl ethers were separated from the vinylated products by flash chromatography.

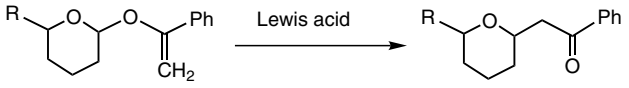
We were unable to synthesize vinyl glycosides or ethers containing ester protecting groups by the Gassman method. Side reactions occurred in the case of acetylated sugars during the elimination step, and benzoylated sugars reacted very slowly. However, vinyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside **10** could be obtained in high

yield from the corresponding tetra-*O*-benzyl ether by reductive debenzylation followed by acetylation (Eq. 4).[20]



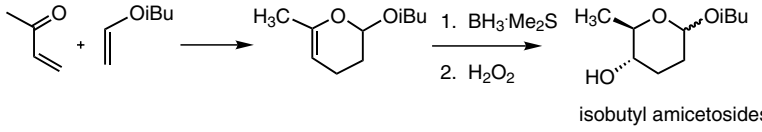
(4)

The synthesis of styryl glycosides by this method was problematic for different reasons. Condensation of tetra-*O*-benzyl-D-glucopyranose with α-methoxystyrene gave good yields of the mixed acetal glycoside; however, the elimination step produced a complex mixture of products, perhaps due to the possibility of rearrangement of the styryl glycosides to carbon-linked glycosides. This rearrangement has been demonstrated for THP-substituted styryl ethers (Eq. 5).[21]



(5)

Aside from the use of vinyl glycosides as chiral auxiliaries in the Bradsher reaction and the cyclobutane synthesis, there have been few examples of the use of vinyl glycosides or other carbohydrate vinyl ethers in cycloaddition reactions, with the exception of glycals.[22] Dujardin et al. have described the asymmetric synthesis of monosaccharides by cycloaddition of unsaturated carbonyl compounds with chiral vinyl ethers derived from noncarbohydrates.[23] Earlier work by Catelani showed that deoxygenated monosaccharides such as amicetose can be synthesized in racemic form by the hetero-Diels–Alder reaction of methyl vinyl ketone and isobutyl vinyl ether, followed by hydroboration–oxidation (Eq. 6).[24]



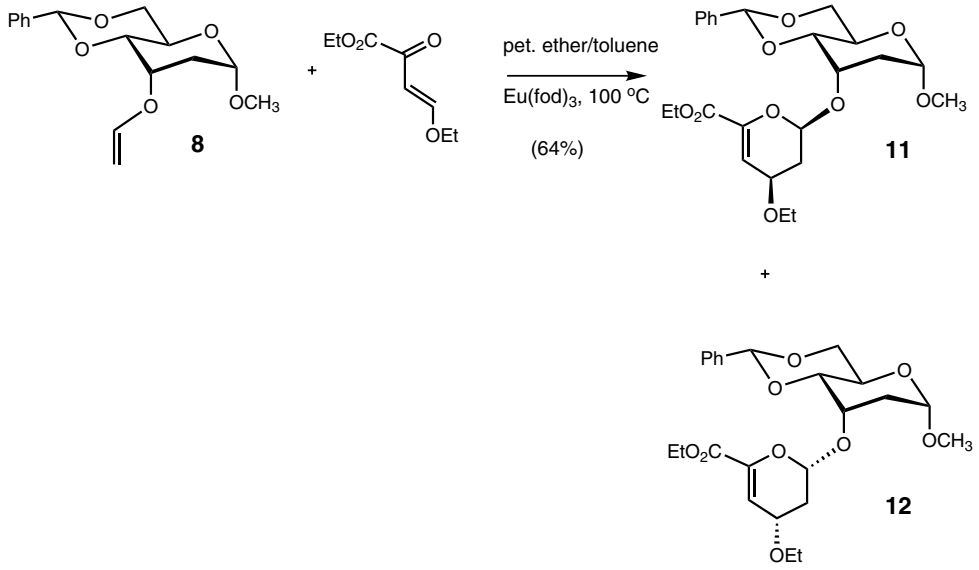
(6)

During the course of our studies of the synthesis of carbohydrate components of antibiotics, it occurred to us that highly deoxygenated sugars[25] such as amicetose or rhodinose could be constructed onto sugar templates by a hetero-Diels–Alder reaction of a carbohydrate vinyl ether with an unsaturated carbonyl compound. The resulting cycloadducts can then be transformed into oligosaccharide components of antibiotics. Among possible hetero-dienes to explore the feasibility of this approach, we chose ethyl (*E*)-ethoxymethylenepyruvate because of it had been shown previously to undergo cycloadditions with vinyl ethers, as a route to deoxy sugars[23] and the lactone moiety of compactin.[26,27] Synthesis of a disaccharide by this approach requires that the carbohydrate vinyl ether undergo cycloaddition efficiently with a suitable heterodiene, with functionality that can be further elaborated to the deoxy sugar. Because two new stereogenic centers are formed in this reaction, there are four possible products, assuming a unique regiochemistry for the cycloaddition step. When **8** was treated with ethyl (*E*)-ethoxymethylenepyruvate in the presence of a catalyst, a 64% yield of two cycloadducts was obtained (Scheme 2). The products were formed in equal amounts. Structures for these were assigned as **11** and **12** based on extensive NMR analysis, including 2D and NOE difference spectroscopy. Irradiation of the anomeric proton on the unsaturated ring resulted in a 7% enhancement of the C-3 proton on this ring. The other product was assumed to have the opposite configuration at these two newly formed stereogenic centers. The resulting stereochemistry in both cycloadducts is consistent with literature precedent and results from *endo*-addition from the two heterodienophile faces.[23] Similarly, cycloaddition of 6-*O*-vinyl ether **6** with the same heterodiene gave cycloadducts **13** and **14** in 53% yield, which were also assigned as the *endo*-adducts. The functionality present in these cycloadducts, while amenable to conversion to a disaccharide, is not well suited for the synthesis of disaccharides of antibiotics that contain rhodinose or amicetose, because of the additional transformations that would be required. A number of steps would be required to modify the ester group in the heterodiene, and the ethoxy group would be difficult to work with. It should be possible; however, to carry out the cycloaddition step with other heterodienes as well as with different carbohydrate substrates that would more closely resemble the final sugar residues in the antibiotics. Further studies of the cycloaddition of carbohydrate vinyl ethers with heterodienes are in progress.

2. Experimental

2.1. General methods

^{1}H NMR spectra were recorded at 300 MHz with TMS as an internal reference in $CDCl_3$, and ^{13}C NMR spectra were recorded at 75 MHz and referenced with $CDCl_3$, unless otherwise noted. Melting points were determined in an open capillary tube with a Thomas Hoover apparatus and are uncorrected. TLC analyses were con-



Scheme 2. Hetero-Diels–Alder approach to 3-*O*-linked deoxy disaccharides.

ducted on aluminum-backed silica gel Kieselgel 60 F254 plates and visualized by UV254 nm or with ammonium molybdate–ceric sulfate reagent. Flash chromatography[28] was carried out with 'Baker' silica gel. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter as $[\alpha]_D$ values at 23 °C. Elemental analyses were carried out at Robertson Microlit Laboratories. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Laboratory, using electrospray ionization.

2.2. General procedure of the preparation of mixed acetals

Ethyl vinyl ether (5 M equiv) and PPTS (10 mg/mmol of carbohydrate substrate) were added to a solution the starting carbohydrate in dry dichloromethane (10 mL/mol) and the mixture was stirred at room temperature for 1–2 h. Progress of the reaction was monitored by TLC using 20% ethyl acetate/hexanes; the mixed acetals had much higher R_f values than the starting carbohydrates (see below). Solid $NaHCO_3$ (1 g) was added and after stirring 10 min, the mixture was filtered, dried ($MgSO_4$), and concentrated to an oil containing a mixture of two diastereomeric mixed acetals. The product was used directly for preparation of the vinyl glycosides and carbohydrate vinyl ethers; however, by flash chromatography over Florisil gave analytically pure products.

2.3. 1-Ethoxyethyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside 1

From 1.5 g (2.77 mmol) of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose there was obtained 1.58 g (93%) of mixed acetal glycoside **1** as an inseparable mixture of diastereomers: R_f 0.44 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +29.2 (*c* 0.61, chloroform), ^{1}H NMR[29] (major isomer) δ 7.36–7.12 (m, 20H, Ph–H), 5.17 (d, 1H, $J_{1,2}$ 3.7, H-1), 4.91 (ABq, 2H, *J* 10.9, $PhCH_2$), 4.90 (q, 1H, *J* 5.3, $OCHCH_3$), 4.73 (ABq, 2H, *J* 11.8, $PhCH_2$), 4.66 (ABq, 2H, *J* 10.9, $PhCH_2$), 4.54 (ABq, 2H, *J* 12.2, $PhCH_2$), 4.03 (dd, $J_{3,4}$ 9.0, H-3), 3.83 (dddd, 1H, $J_{1,5}$ 0.6, $J_{5,4}$ 10.0, $J_{5,6}$ 3.4, $J_{5,6'}$ 1.9, H-5), 3.73 (dq, 1H, *J* 9.3, 7.1, OCH_2CH_3), 3.73 (dq, 1H, H-6′), 3.65 (dd, 1H, $J_{4,3}$ 9.0, H-4), 3.61 (dd, 1H, $J_{6,6'}$ 10.6, H-6), 3.60 (dd 1H, $J_{2,3}$ 9.7, H-2), 3.50 (dq, 1H, OCH_2CH_3), 1.37 (d, 3H, $OCHCH_3$), 1.17 (t, 3H, OCH_2CH_3); ^{13}C NMR (major isomer) δ 138.8–137.8, 128.3–127.7, 98.3, 94.0, 82.0, 79.6, 77.8, 75.5, 75.0, 73.4, 73.1, 70.6, 68.5, 60.8, 20.8, 15.1; ^{1}H NMR (minor isomer) δ 7.36–7.12 (m, 20H, Ph–H), 5.17 (d, 1H, $J_{1,2}$ 3.7, H-1), 4.91 (ABq, 2H, *J* 10.9, $PhCH_2$), 4.84 (q, 1H, *J* 5.3, $OCHCH_3$), 4.72 (ABq, 2H, *J* 11.8, $PhCH_2$), 4.83 (ABq, 2H, *J* 10.9, $PhCH_2$), 4.53 (ABq, 2H, *J* 12.2, $PhCH_2$), 4.02 (dd, $J_{3,4}$ 9.0, H-3), 3.96 (dddd, 1H, $J_{1,5}$ 0.5, $J_{5,4}$ 10.0, $J_{5,6}$ 3.6, $J_{5,6'}$ 2.2, H-5), 3.86 (dq, 1H, *J* 9.3, 7.1, OCH_2CH_3), 3.74 (dq, 1H, H-6′), 3.67 (dd, 1H, $J_{4,3}$ 9.0, H-4), 3.60 (dd, 1H, $J_{6,6'}$ 10.6, H-6), 3.57 (dd 1H, $J_{2,3}$ 9.7, H-2), 3.43 (dq, 1H, OCH_2CH_3), 1.38 (d, 3H, $OCHCH_3$), 1.13 (t, 3H, OCH_2CH_3); ^{13}C NMR (major isomer) δ 138.8–137.8, 128.3–127.7, 99.9, 92.4, 82.0, 79.9, 77.8, 75.5, 74.8, 73.4, 73.1, 70.6, 68.6, 62.8, 20.9, 14.9. Anal. Calcd for $C_{38}H_{44}O_7$: C, 74.48; H, 7.24. Found: C, 74.69; H, 7.19.

2.4. 1-Methoxy-1-methylethyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside 3

To a solution of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (0.54 g, 1 mmol) in anhydrous dichloromethane (20 mL) was added pyridinium *p*-toluenesulfonate (10 mg) and 2-methoxypropene (0.5 mL, 5 equiv) and the mixture was stirred at room temperature for 2 h. Solid sodium carbonate was added and after stirring briefly, the mixture was filtered and the filtrate concentrated to an oil, which was dried under vacuum (0.635 g, quantitative): $[\alpha]_D$ = +60 (*c* 1.1, chloroform), ^{1}H NMR δ 7.35–7.11 (m, 20H, Ph–H), 5.36 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.92 (ABq, 2H, *J* 10.9, $PhCH_2$), 4.72 (ABq, 2H, *J* 11.6, $PhCH_2$), 4.65 (ABq, 2H, *J* 10.6,

$PhCH_2$), 4.55 (ABq, 2H, J 12.2, $PhCH_2$), 4.04 (dd, $J_{3,4}$ 9.0, H-3), 3.92 (ddd, 1H, $J_{5,4}$ 10.0, $J_{5,6}$ 3.6, $J_{5,6'}$ 2.0, H-5), 3.75 (dd, 1H, $J_{6,6'}$ 10.5, H-6), 3.68 (dd, 1H, $J_{4,3}$ 10.0, H-4), 3.60 (dd, 1H, H-6′), 3.58 (dd 1H, $J_{2,3}$ 9.8, H-2), 3.28 (s, 3H, OCH_3), 1.43 (s, 3H, CH_3), 1.38 (s, 3H, CH_3); ^{13}C NMR δ 138.9–137.3 (4C), 128.4–127.4 (20C), 101.1 (CMe_2), 89.8 (C-1), 82.0 (C-3), 80.1 (C-2), 78.0 (C-4), 75.4 ($PhCH_2$), 75.0 ($PhCH_2$), 73.4 ($PhCH_2$), 73.3 ($PhCH_2$), 70.2 (C-5), 68.7 (C-6), 49.3 (OCH_3), 26.4 (CH_3), 24.6 (CH_3). HRMS (ES+) Anal. Calcd for $C_{38}H_{44}O_7Na$ [M+Na]: 635.3009. Found: 635.2985.

2.5. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(1-ethoxyethyl)-α-D-glucopyranoside 5

From 0.271 g (0.585 mmol) of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[30] there was obtained 0.311 g (99%) of mixed acetal **5** as a mixture of inseparable diastereomers: R_f 0.30 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +44 (*c* 1.0, chloroform), ^{1}H NMR (major isomer) δ 7.37–7.28 (m, 15H, Ph–H), 4.86 (ABq, 2H, J 10.8, $PhCH_2$), 4.78 (ABq, 2H, J 11.0, $PhCH_2$), 4.73 (ABq, 2H, J 12.3, $PhCH_2$), 4.72 (q, 1H, J 5.4, $OCHCH_3$), 4.62 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.00 (dd, 1H, J 9.8, 8.8, H-3), 3.79 (dd, 1H, $J_{6,6'}$ 10.8, $J_{5,6'}$ 1.6, H-6), 3.725 (m, 1H, H-5), 3.64 (dq, 1H, J 9.5, 7.1 OCH_2CH_3), 3.60 (dd, 1H, $J_{6,6'}$ 10.6, H-6′), 3.54 (m, 1H, H-4), 3.54 (m, 1H, H-2), 3.44 (dq, 1H, OCH_2CH_3), 3.37 (3, 3H, OCH_3), 1.29 (d, 1H, $OCHCH_3$), 1.16 (t, 3H, OCH_2CH_3); ^{1}H NMR (minor isomer) δ 7.37–7.28 (m, 15H, Ph–H), 4.90 (ABq, 2H, J 10.8, $PhCH_2$), 4.75 (ABq, 2H, J 11.0, $PhCH_2$), 4.73 (ABq, 2H, J 12.3, $PhCH_2$), 4.66 (q, 1H, J 5.4, $OCHCH_3$), 4.62 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.00 (dd, 1H, J 9.8, 8.8, H-3), 3.80 (dd, 1H, $J_{6,6'}$ 10.6, $J_{5,6'}$ 3.6, H-6), 3.725 (m, 1H, H-5), 3.60 (dd, 1H, $J_{6,6'}$ 10.6, H-6′), 3.57 (dq, 1H, J 9.3, 7.1 OCH_2CH_3), 3.54 (m, 1H, H-4), 3.54 (m, 1H, H-2), 3.46 (dq, 1H, OCH_2CH_3), 3.38 (3, 3H, OCH_3), 1.29 (d, 1H, $OCHCH_3$), 1.15 (t, 3H, OCH_2CH_3). Anal. Calcd for $C_{31}H_{38}O_7$: C, 71.24; H, 7.33. Found: C, 71.27; H, 7.46.

2.6. Methyl 4,6-*O*-benzylidene-3-*O*-(1-ethoxyethyl)-2-deoxy-α-D-*ribo*-hexopyranoside 7

From 1.29 g (4.84 mmol) of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside[31] there was obtained 1.51 g (92%) of mixed acetal **7** as a mixture of inseparable diastereomers: R_f 0.16 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +201 (*c* 1.0, chloroform), ^{1}H NMR (major isomer) δ 7.49–7.39 (m, 5H, Ph–H), 5.54 (s, 1H, PhC*H*), 4.89 (q, 1H, J 5.3, $OCHCH_3$), 4.70 (dd, 1H, $J_{1,2eq}$ 0.7, $J_{1,2ax}$ 4.5, H-1), 4.29 (m, 2H, H-5, H-6), 4.18 (1H, $J_{3,4}$ 2.5, H-3), 3.69 (t, 1H, $J_{6,6'}$ 12.0, H-6′), 3.69 (dq, 1H, J 9.0, 7.1 OCH_2CH_3), 3.63 (dd, 1H, $J_{4,5}$ 9.3, H-4), 3.44 (dq, 1H, OCH_2CH_3), 3.37 (s, 3H, OCH_3), 2.16 (ddd, 1H, $J_{2eq,3}$ 2.7, H-2eq), 2.02 (ddd, 1H, $J_{2ax,3}$ 3.9, H-2ax), 1.37 (d, 1H, $OCHCH_3$), 1.12 (t, 3H, OCH_2CH_3); ^{13}C NMR (major isomer) δ 137.7, 128.9, 128.1, 126.1, 101.9, 101.1, 97.8, 79.8, 69.5, 68.9, 60.2, 57.9, 55.3, 35.4, 20.7, 15.2; ^{1}H NMR (minor isomer) δ 7.49–7.39 (m, 5H, Ph–H), 5.56 (s, 1H, PhC*H*), 4.92 (q, 1H, J 5.4, $OCHCH_3$), 4.70 (dd, 1H, $J_{1,2eq}$ 0.8, $J_{1,2ax}$ 4.6, H-1), 4.29 (m, 2H, H-5, H-6), 4.15 (q, 1H, $J_{3,4}$ 2.5, H-3), 3.69 (t, 1H, $J_{6,6'}$ 12.1, H-6′), 3.79 (dq, 1H, J 9.4, OCH_2CH_3), 3.62 (dd, 1H, $J_{4,5}$ 9.3, H-4), 3.57 (dq, 1H, OCH_2CH_3), 3.36 (s, 3H, OCH_3), 2.16 (ddd, 1H, $J_{2eq,3}$ 2.8, H-2eq), 1.91 (ddd, 1H, $J_{2ax,3}$ 3.4, H-2ax), 1.32 (d, 1H, $OCHCH_3$), 1.11 (t, 3H, OCH_2CH_3); ^{13}C NMR (minor isomer) δ 137.8, 128.9, 128.0, 126.1, 101.8, 98.1, 97.9, 79.2, 69.6, 66.0, 60.0, 58.1, 55.3, 34.2, 19.9, 15.1. Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.55; H, 7.53.

2.7. Vinyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside 2

To a solution of acetal **1** (1.75 g, 2.86 mmol) in anhydrous dichloromethane (10 mL) at 0 °C under nitrogen was added freshly distilled triethylamine (0.3 g, 2.97 mmol) followed by trimethylsilyltrifluoromethanesulfonate (0.689 g, 2.92 mmol) over a 5 min period. After 1 h, 1.0 M NaOH (4 mL) was added followed by diethyl ether (15 mL). The organic phase was separated, dried ($MgSO_4$) and concentrated to an oil (1.74 g), which was purified by flash chromatography on silica gel using 20% ethyl acetate/hexanes to give vinyl glycoside **2**; yield, 0.83 g (51%). In a different run, 1.25 g (2.04 mmol) of mixed acetal was treated with 1.5 equiv of triethylamine and 1.3 equiv of TMS-triflate overnight at room temperature, to give 388 mg (68%) of vinyl glycoside after purification by flash chromatography: R_f 0.25 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +30.2 (*c* 0.7, chloroform), lit.[10] $[\alpha]_D^{21}$ = +30.9 (*c* 1.12, chloroform); ^{1}H NMR (major isomer) δ 7.37–7.10 (m, 20H, Ph–H), 6.36 (dd, 1H, J 14.2, 6.5, vinyl), 5.07 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.92 (ABq, 2H, J 10.8, $PhCH_2$), 4.72 (ABq, 2H, J 12.2, $PhCH_2$), 4.65 (ABq, 2H, J 10.9, $PhCH_2$), 4.62 (dd, 1H, J 1.7, 14.2, vinyl), 4.51 (ABq, 2H, J 12.0, $PhCH_2$), 4.21 (dd, 1H, vinyl), 4.05 (dd, 1H, $J_{3,2}$ 9.6, $J_{3,4}$ 8.3, H-3), 3.73 (m, 3H, H-5, H-6), 3.61 (dd, 1H, H-2), 3.59 (m, 1H, H-6′); ^{13}C NMR δ 138.6–137.7, 128.3–127.4, 148.4 (vinyl), 96.1 (C-1), 92.4 (vinyl), 81.8 (C-3), 79.2 (C-2), 77.2 (C-4), 75.6 ($PhCH_2$), 74.9 ($PhCH_2$), 73.3 ($PhCH_2$), 73.2 ($PhCH_2$), 70.1 (C-5), 68.0 (C-6). Anal. Calcd for $C_{37}H_{40}O_5$: C, 76.30; H, 6.76. Found: C, 76.45; H, 6.59.

2.8. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-vinyl-α-D-glucopyranoside 6

To a solution of acetal **5** (0.58 g, 1.08 mmol) in anhydrous dichloromethane (3.5 mL) at 0 °C was added freshly distilled triethylamine (0.12 g, 1.19 mmol) followed by trimethylsilyltrifluoromethanesulfonate (0.269 g, 1.14 mmol) over a 5 min period. After 40 min, 1.0 M NaOH (4 mL) was added followed by diethyl ether (25 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated to an oil (0.431 g), which was purified by flash chromatography on silica gel using 20% ethyl acetate/hexanes to give analytically pure vinyl ether **6**; yield, 0.112 g (21%): R_f 0.48 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +16.7 (*c* 1.0, chloroform), ^{1}H NMR (major isomer) δ 7.38–7.24 (m, 15H, Ph–H), 6.48 (dd, 1H, vinyl), 4.92 (ABq, 2H, J 10.9, $PhCH_2$), 4.72 (ABq, 2H, J 11.6, $PhCH_2$), 4.65 (ABq, 2H, J 10.6, $PhCH_2$), 4.60 (d, 1H, $J_{1,2}$ 3.6, H-1), 4.18 (dd, 1H,

vinyl), 4.02 (dd, 1H, vinyl), 4.00 (dd, 1H, $J_{3,2}$ 9.6, $J_{3,4}$ 9.4, H-3), 3.90–3.78 (m, 3H, H-5, H-6, H-6′), 3.59 (dd, 1H, $J_{4,5}$ 9.0, H-4), 3.55 (dd, 1H, H-2), 3.37 (s, 3H, OCH_3); ^{13}C NMR δ 138.7–138.1 (3C), 128.4–127.5 (15C, Ph), 151.5 (vinyl), 98.2 (C-1), 87.0 (vinyl), 82.0 (C-3), 79.8 (C-2), 77.4 (C-4), 75.7 ($PhCH_2$), 75.1 ($PhCH_2$), 73.4 ($PhCH_2$), 69.0 (C-5), 66.3 (C-6), 55.2 (OCH_3). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.27, 7.12.

2.9. Isopropenyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside 4

To a solution of 1-methoxy-1-methylethyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside **3** (0.61 g, 0.97 mmol) in anhydrous dichloromethane (3 mL) was added triethylamine (0.216 mL, 1.6 equiv) and, at 0 °C, trimethylsilyltrifluorormethanesulfonate (0.297 g, 1.3 equiv) under nitrogen and the mixture was stirred overnight at room temperature. TLC (30% ethyl acetate/hexane) showed the presence of starting material so additional triethylamine (54 μL) and TMS-triflate (0.31 μL) were added and the reaction was again stirred at rt overnight. Aqueous sodium hydroxide solution (1 mL of 1.0) was added followed by diethyl ether (50 mL). The mixture was shaken and the organic phase separated, dried (Na_2SO_4), and concentrated to a residue, which was purified by flash chromatography using 20% ethyl acetate/hexanes to give 0.318 g (56%) of isopropenyl glycoside **4** as a syrup: R_f 0.53 (20% ethyl acetate/hexanes). The ^1H NMR spectrum matched that reported[4] except for one of the vinyl resonances, which the authors reported and 4.24 and we assigned at 4.04: ^1H NMR δ 7.37–7.10 (m, 5H, Ph–H), 5.32 (d, 1H, $J_{1,2}$ 3.6, H-1), 4.92 (ABq, 2H, J 10.6, $PhCH_2$), 4.70 (ABq, 2H, J 12.0, $PhCH_2$), 4.65 (ABq, 2H, J 10.6, $PhCH_2$), 4.53 (ABq, 2H, J 12.2, $PhCH_2$), 4.29 (dd, 1H, J 1.6, vinyl), 4.04 (dq, 1H, J 1.6, 1.0 vinyl), 4.03 (dd, 1H, $J_{3,2}$ 9.6, $J_{3,4}$ 8.7, H-3), 3.79–3.72 (m, 3H, H-4, H-5, H-6), 3.63 (dd, 1H, H-2), 3.59 (m, 1H, H-6′), 1.86 (d, 3H, J 1.0, CH_3).

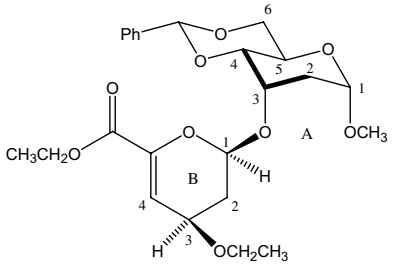
2.10. Methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-vinyl-α-D-*ribo*-hexopyranoside 8

To a solution of acetal **7** (0.824 g, 2.43 mmol) in anhydrous dichloromethane (11 mL) at 0 °C was added freshly distilled triethylamine (0.258 g, 2.55 mmol) followed by trimethylsilyltrifluoromethanesulfonate (0.591 g, 2.5 mmol) over a 5 min period. After 40 min, 1.0 M NaOH (4 mL) was added followed by diethyl ether (25 mL). The organic phase was separated, dried ($MgSO_4$) and concentrated to an oil (0.617 g), which was purified by flash chromatography on silica gel using 20% ethyl acetate/hexanes to give solid 3-*O*-vinyl ether; yield, 0.396 g (56%): R_f 0.25 (20% ethyl acetate/hexanes), $[\alpha]_D$ = +104.2 (*c* 1.0, chloroform), ^1H NMR (major isomer) δ 7.43–7.33 (m, 5H, Ph–H), 6.41 (dd, 1H, J 14.1, 6.6, vinyl), 5.56 (s, 1H, PhC*H*), 4.72 (d, 1H, $J_{1,2a}$ 4.6, $J_{1,2e}$ 0.7, H-1), 4.38 (dd, 1H, vinyl), 4.33 (m, 1H, $J_{5,6}$ 5.4, $J_{5,6'}$ 12.2, H-5), 4.31 (m, 1H, $J_{3,4}$ 2.9, H-3), 4.30 (dd, 1H, $J_{6,6'}$ 12.2, H-6), 4.04 (dd, 1H, vinyl), 3.71 (t, 1H, H-6′), 3.70 (dd, 1H, $J_{4,5}$ 9.5, H-4), 3.38 (s, 3H, OCH_3), 2.31 (ddd, 1H, $J_{2e,3}$ 2.8, $J_{2e,2a}$ 15.1, H-2e), 1.98 (ddd, 1H, $J_{2a,3}$ 3.7, H-2a); ^{13}C NMR δ 152.7, 137.5, 129.0, 128.2, 126.3, 103.1, 97.6, 88.4, 78.9, 71.4, 69.4, 58.0, 55.3, 33.5. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.43, 6.88.

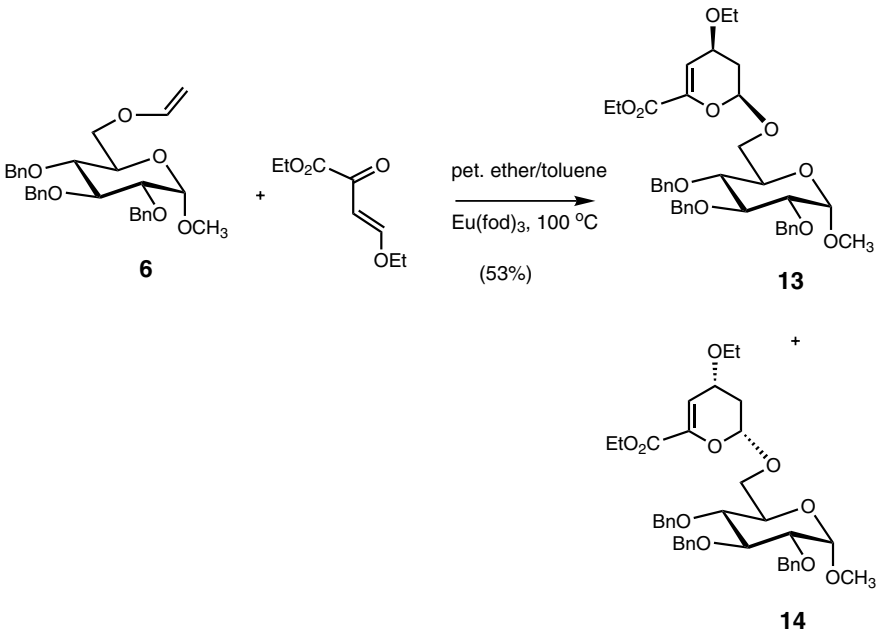
2.11. Vinyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside 10

Freshly cut sodium (212 mg, 9.22 mmol) was added in small pieces to liquid ammonia (15 mL) at −43 °C (acetonitrile–dry ice bath). Approximately one-half of the sodium was added to produce a blue color, followed by a solution of vinyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside **2** (300 mg, 0.53 mmol) in dry THF (1.5 mL), and then the remaining sodium was added. The mixture was stirred at −43 °C for 6 h. Solid ammonium chloride was added and the mixture was allowed to warm to room temperature. Remaining ammonia was allowed to evaporate using a stream of argon, and then dry pyridine (93 mL) was added followed by acetic anhydride (1.0 mL) and the mixture was stirred overnight at room temperature. The reaction was diluted with dichloromethane (20 mL) and then washed with satd aq $NaHCO_3$. The organic phase was washed with water, satd aq NaCl, dried (Na_2SO_4), and concentrated to an oil that was purified by flash chromatography on a

Table 2. ^1H data for hetero-Diels–Alder adduct **11**

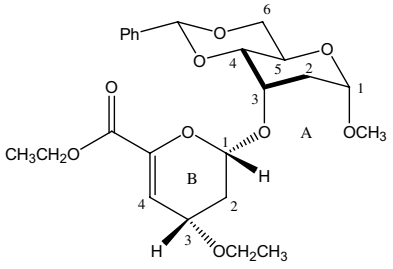


^1H A-ring	δ (ppm)	^1H B-ring	δ (ppm)
1	4.69d	1	5.35dd
2ax	2.05ddd	2	2.34dddd
2eq	2.32ddd	2′	2.06dt
3	4.40q	3	4.13dt
4	3.68dd	4	6.04dd
5	4.30m	$CH_3CH_2O_2C$	4.24, 4.92 cm
6	4.30m	$CH_3CH_2O_2C$	1.28t
6′	3.71t	CH_3CH_2O	3.55, 3.49 cm
OCH_3	3.34s	CH_3CH_2O	1.21t
PhCH	5.56s		
Ph–H	*o* 7.45m; *m*,*p* 7.38–7.35m		
J	Hz	*J*	Hz
1, 2ax	4.5	1, 2	2.5
1, 2eq	0.6	1, 2′	7.9
2ax, 2eq	15.2	2, 2′	13.3
2ax, 3	4.0	2, 3	6.8
2eq, 3	2.9	2′, 4	1.2
3, 4	2.9	2′, 3	7.9
3, 1 (B-ring)	Not measured	$CH_3CH_2O_2C$	10.8
4, 5	9.1	$CH_3CH_2O_2C$	7.2
5, 6	Not measured	CH_3CH_2O	8.9
5, 6′	12.0	CH_3CH_2O	7.0
6, 6′	12.0	3, 4	3.0



Scheme 3. Hetero-Diels–Alder approach to 6-*O*-linked deoxy disaccharides.

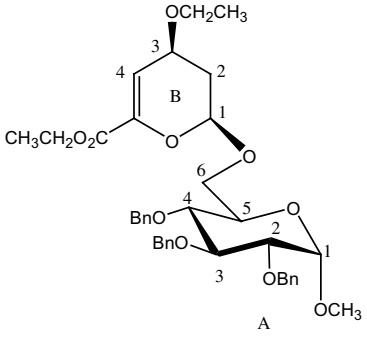
Table 3. ^{1}H NMR data for hetero-Diels–Alder adduct **12**



^{1}H A-ring	δ (ppm)	^{1}H B-ring	δ (ppm)
1	4.66d	1	5.47dd
2ax	1.99ddd	2	2.24m
2eq	2.14ddd	2′	1.86ddd
3	4.40q	3	4.29m
4	3.66dd	4	6.18dd
5	4.29m	$CH_3CH_2O_2C$	4.26–4.22m
6	4.29m	$CH_3CH_2O_2C$	1.30t
6′	3.71t	CH_3CH_2O	3.59–3.54m
OCH_3	3.32s	CH_3CH_2O	1.20t
PhCH	5.56 s		
Ph–H	*o* 7.45m; *m*,*p* 7.38–7.33m		
J	Hz	*J*	Hz
1, 2ax	4.3	1, 2	4.3
1, 2eq	0.9	1, 2′	2.6
2ax, 2eq	15.1	2, 2′	13.1
2ax, 3	3.8	2, 3	5.9
2eq, 3	3.0	2, 4	1.2
3, 4	2.8	2′, 3	8.6
3, 1(B-ring)	0.5	$CH_3CH_2O_2C$	10.8
4, 5	9.0	$CH_3CH_2O_2C$	7.1
5, 6	Not measured	CH_3CH_2O	9.1
5, 6′	12.1	CH_3CH_2O	7.0
6, 6′	12.1	3, 4	2.9

30 mm × 20 cm column of silica gel using 20% ethyl acetate/hexane. There was obtained 205 mg (quantitative) of solid tetraacetate **10**: mp 103–105 °C lit.[9a] mp 105 °C; $[\alpha]_D = +129.8$ (*c* 0.5, chloroform), lit.[9a] $[\alpha]_D^{21} = +135.4$

Table 4. ^{1}H NMR data for hetero-Diels–Alder adduct **13**



^{1}H A-ring	δ (ppm)	^{1}H B-ring	δ (ppm)
1	4.58d	1	4.96dd
2	3.5	2, 2′	2.04m
3	3.99t	3	4.04dd
4	3.5	4	6.12dd
5	3.78m	$CH_3CH_2O_2C$	4.21, q
6	4.14dd	$CH_3CH_2O_2C$	1.27t
6′	3.67dd	CH_3CH_2O	3.52m
OCH_3	3.36s	CH_3CH_2O	1.18t
$PhCH_2$	4.90, 4.73, 4.72, ABq		
Ph–H	7.36–7.28		
J	Hz	*J*	Hz
1, 2	3.4	1, 2	3.3
2, 3	Not measured	1, 2′	6.2
3, 4	Not measured	2, 3, 2′, 3	6.6
		$CH_3CH_2O_2C$	Not measured
4, 5	10.0	$CH_3CH_2O_2C$	7.1
5, 6	1.8	CH_3CH_2O	Not measured
5, 6′	5.2	CH_3CH_2O	6.9
6, 6′	10.8	3, 4	3.3

(c 1, chloroform); R_f 0.34 (20% ethyl acetate/hexanes); the ^{1}H NMR spectrum of **9** matched that reported.[9a]

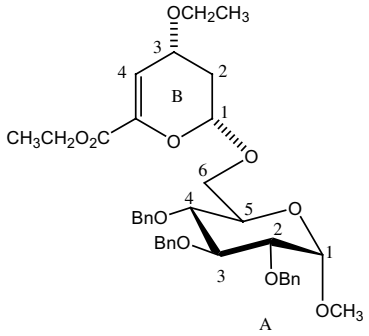
2.12. Methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-(ethyl 2,4-dideoxy-3-*O*-ethyl-α-D/L-*glycero*-hex-4-enopyranosyluronate)-α-D-*ribo*-hexopyranoside 11 and 12

A mixture of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-vinyl-α-D-*ribo*-hexopyranoside **8** (150 mg, 0.5 mmol), ethyl (*E*)-ethoxymethylenepyruvate[26] (91 mg, 0.53 mmol), and Eu(fod)$_3$ (20 mg, 0.019 mmol) in 900 μL petroleum ether/100 μL toluene was heated in a thick-walled reaction tube fitted with a Teflon screw cap under nitrogen at 100 °C for 2 days. TLC (30% ethyl acetate/hexanes) showed complete consumption of starting materials. The sample was diluted with toluene (2 mL) and concentrated to an oil. Flash chromatography afforded cycloadducts **11** (74 mg) and **12** (79 mg) with R_f 0.28 and R_f 0.41 (30% ethyl acetate/hexanes); combined yield, 64%. ^{1}H NMR data are shown in Tables 2 and 3. HRMS (ES+) Anal. Calcd for $C_{24}H_{32}O_9Na$ [M+Na]: 487.1944. Found: 487.1939 (Scheme 3).

2.13. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(ethyl 2,4-dideoxy-3-*O*-ethyl-α-D/L-*glycero*-hex-4-enopyranosyluronate)-α-D-glucopyranoside 13 and 14

A mixture of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **6** (112 mg, 0.228 mmol), ethyl (*E*)-ethoxymethylenepyruvate[26] (39.2 mg, 0.228 mmol), and Eu(fod)$_3$ (15 mg, 0.014 mmol) in 900 μL petroleum ether/100 μL toluene was heated in a thick-walled reaction tube fitted with a Teflon screw cap under nitrogen at 100 °C for 3 days. TLC (1:1 ethyl acetate/hexanes) showed complete consumption of starting materials. The sample was diluted with toluene (2 mL) and concentrated to an oil (0.140 g). Flash chromatography afforded cycloadducts **13** and **14** with R_f 0.50 and R_f 0.62 (1:1 ethyl acetate/hexanes); combined yield, 80.1 mg (53%). Rechromatography of the cycloadduct mixture gave enriched fractions for NMR analysis. ^{1}H NMR data are shown in Tables 4 and 5. HRMS (ES+) Anal. Calcd for $C_{38}H_{46}O_{10}Na$ [M+Na]: 685.2989. Found: 685.2993.

Table 5. ^{1}H NMR data for hetero-Diels–Alder adduct **14**



A

^{1}H A-ring	δ (ppm)	^{1}H B-ring	δ (ppm)
1	4.60d	1	5.27dd
2	3.5dd	2, 2′	2.14m
3	3.96t	3	4.21dd
4	3.67t	4	6.18d
5	3.77–3.70m	$CH_3CH_2O_2C$	4.13, 4.11q
6	3.77–3.70m	$CH_3CH_2O_2C$	1.20t
6′	3.77–3.70m	CH_3CH_2O	3.53q
OCH_3	3.36s	CH_3CH_2O	1.19t
$PhCH_2$	4.89, 4.74, 4.73, ABq		
Ph–H	7.37–7.25m		
J	Hz	J	Hz
1, 2	3.6	1, 2	5.0
2, 3	9.8	1, 2′	3.4
3, 4	8.5	2, 3, 2′,3	Not measured
		$CH_3CH_2O_2C$	10.8
4, 5	8.5	$CH_3CH_2O_2C$	7.1
5, 6	Not measured	CH_3CH_2O	Not measured
5, 6′	Not measured	CH_3CH_2O	6.9
6, 6′	Not measured	3, 4	3.8

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References

1. Choudhury, A.; Franck, R. W.; Gupta, R. B. *Tetrahedron Lett.* **1989**, *37*, 4921–4924.
2. Ganz, I.; Kunz, H. *Synthesis* **1994**, 1353–1358.
3. de Raadt, A.; Ferrier, R. J. *Carbohydr. Res.* **1991**, *216*, 93–107.
4. Marra, A.; Esnault, J.; Veyrieres, A.; Sinaÿ, P. *J. Am. Chem. Soc.* **1992**, *114*, 6354–6360.
5. (a) Boons, G.-J.; Heskamp, B.; Hout, F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2845–2847; (b) Boons, G. J.; Isles, S. *J. Org. Chem.* **1996**, *61*, 4262–4271.
6. Wang, W.; Zhang, Y.; Zhou, H.; Bleriot, Y.; Sinaÿ, P. *Eur. J. Org. Chem.* **2001**, *6*, 1053–1059.
7. Godage, H. Y.; Fairbanks, A. J. *Tetrahedron Lett.* **2000**, *41*, 7589–7593.
8. Ennis, S. C.; Fairbanks, A. J.; Slinn, C. A.; Tennant-Eyles, R. J.; Yeates, H. S. *Tetrahedron* **2001**, *57*, 4221–4230.
9. (a) Dettinger, H.-M.; Lehman, J.; Wallenfals, K. *Carbohydr. Res.* **1980**, *87*, 63–70; (b) Tietze, L. F.; Fischer, R.; Guder, H. J.; Goerlach, A.; Neumann, M.; Krach, T. *Carbohydr. Res.* **1987**, *164*, 177–194.
10. Perrine, T. D.; Glaudemans, C. P. J.; Ness, R. K.; Kyle, J.; Fletcher, H. G., Jr. *J. Org. Chem.* **1967**, *32*, 664–669.
11. de Raadt, A.; Ferrier, R. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1009–1010.
12. Rollin, P.; Verez Bencomo, V.; Sinaÿ, P. *Synthesis* **1984**, 134–135.
13. Cottier, L.; Remy, G.; Descotes, G. *Synthesis* **1979**, 711–712.
14. Handerson, S.; Schlaf, M. *Org. Lett.* **2002**, *4*, 407–409.
15. Reinhart, K. L., Jr.; Beck, J. R.; Borders, D. B.; Kinstle, T. H.; Krauss, D. *J. Am. Chem. Soc.*
16. Gassman, P.; Burns, S. J.; Pfister, K. B. *J. Org. Chem.* **1993**, *58*, 1449–1457.
17. Dujardin, G.; Rossignol, S.; Brown, E. *Tetrahedron Lett.* **1995**, *36*, 1653–1656.
18. Tietze, L. F.; Logers, M. *Liebigs Ann. Chem.* **1990**, 261–265.
19. Edathil, J.; Nguyen, J.; Hughes, K.; Boyko, W. J.; Giuliano, R. M. *J. Carbohydr. Chem.* **2001**, *20*, 81–85.
20. Ceccherelli, P.; Coccia, R.; Curini, M.; Pelicciari, R. *Gazz. Chim. Ital.* **1983**, *113*, 453–455.

21. Zhang, Y.; Reynolds, N. T.; Manju, K.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 9720–9721.
22. Chmielewski, M.; Kaluza, Z.; Grodner, J.; Urbanski, R. In *Cycloaddition Reactions in Carbohydrate Chemistry*; Giuliano, R. M., Ed.; American Chemical: Washington DC, 1992; pp 50–65; Leblanc, Y.; Labelle, M. In *Cycloaddition Reactions in Carbohydrate Chemistry*; Giuliano, R. M., Ed.; American Chemical: Washington DC, 1992; pp 81–96; Lubineau, A.; Auge, J.; Bienayme, H.; Lubin, N.; Queneau, Y. In *Cycloaddition Reactions in Carbohydrate Chemistry*; Giuliano, R. M., Ed.; American Chemical: Washington DC, 1992; pp 147–158.
23. Dujardin, G.; Rossignol, S.; Brown, E. *Tetrahedron Lett.* **1996**, *37*, 4007–4010.
24. Berti, G.; Catelani, G.; Magi, S.; Monti, L. *Gazz. Chim. Ital.* **1980**, *110*, 173.
25. Arcamone, F.; Barbieri, W.; Franceschi, G.; Penco, S.; Vegevani, A. *J. Am. Chem. Soc.* **1973**, *95*, 2008–2009; Arcamone, F.; Franceschi, G.; Gioia, G.; Penco, S.; Vegevani, A. *J. Am. Chem. Soc.* **1973**, *95*, 2009–2011; Stevens, C. L.; Blumbergs, P.; Wood, D. L. *J. Am. Chem. Soc.* **1964**, *86*, 3592–3594.
26. Dujardin, G.; Rossignol, S.; Brown, E. *Synthesis* **1998**, 763–770.
27. These authors have recently developed related methodology for the synthesis of 2-amino glycosides: Gaulon, D.; Dhal, R.; Chapin, T.; Maisonneuve, V.; Dujardin, G. *J. Org. Chem.* **2004**, *69*, 4192–4202.
28. Still, W. C.; Kahn, M.; Mitra, M. *J. Org. Chem.* **1978**, *43*, 2923–2925.
29. ^{1}H and ^{13}C shifts were previously reported[9b] for a few key resonances of mixed acetal **1**, and matched those observed in this study.
30. Eby, R.; Schuerch, C. *Carbohydr. Res.* **1974**, *34*, 79–90.
31. Rosenthal, A.; Catsoulacos, P. *Can. J. Chem.* **1968**, *46*, 2868–2872.