Pergamon

Tetrahedron 56 (2000) 8525–8531

TETRAHEDRON

Synthesis of C-2 Methylene *O*- and *C*-Glycosides and Sugar Derived α-Methylene-δ-valerolactones from C-2-Acetoxymethyl Glycals☆

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Received 12 April 2000; revised 9 August 2000; accepted 23 August 2000

Abstract—C-2-Methylene *O*- and *C*-glycosides are readily synthesized from C-2-acetoxymethyl glycals using Nafion-H®, montmorillonite K-10, $LiClO_4$ (0.07 M) in dichloromethane and $Pd(PPh_3)_4$ as catalysts. Exclusive α or β selectivities have been observed with various primary, secondary and tertiary alcohols, phenols and diethyl malonate. Further, C-2-acetoxymethyl glycals are also converted into corresponding α-methylene-δ-valerolactones in good yields in one step using *m*-CPBA in the presence of $BF_3{\cdot}Et_2O$.

Synthesis of branched chain sugars has gained importance in recent years mainly because of the occurrence of such type of structural units in nature.[1] As a result, efforts have been made to prepare analogs of such branched chain sugars for biological evaluation. Besides this, branched sugars also serve as useful intermediates for the synthesis of other non-sugar chiral molecules. Likewise, sugar derived α-methylene-δ-valerolactones are useful in the synthesis of *C*-glycosides using radical chemistry[2] and α-methylene unit in such lactones also serves as an appendage for branched chain sugar synthesis. In this paper, we present our results pertaining to the synthesis of C-2 methylene *O*- and *C*-glycosides and α-methylene-δ-valerolactones from C-2-acetoxymethy glycals.

Conversion of glycals[3] into C-2 formyl glycals followed by their conversion to C-2-methylene-*O*-glycosides has been reported by Balasubramanian et al.[4] by applying the Ferrier reaction protocol using $BF_3{\cdot}Et_2O$ as a catalyst. In all the cases studied by Balasubramanian et al., α-glycosides were formed as the major products. In an effort to improve the selectivity in such reactions, and possibly reverse the anomeric selectivity, and synthesize *C*-glycosides, we have screened several different types of catalysts. These include two solid acidic catalysts, viz. Nafion-H[5] and montmorillonite K-10[6] and soluble catalysts $LiClO_4$[7] and $Pd(PPh_3)_4$.[8]

Recently,[9] Nafion-H has been employed as a catalyst to effect the Ferrier reaction. In the present study 2-acetoxymethyl glycals **1** and **2** (Scheme 1) and Nafion-H (wt. equiv.) in CH_2Cl_2 gave the corresponding *O*-glycosides **3** in good yields (Table 1) leading to predominantly α-isomers as the corresponding β-isomers, if formed, could not be isolated. Reactions were cleaner in CH_2Cl_2 than in CH_3CN, $CHCl_3$ or Et_2O. The ^1H NMR as well as ^{13}C NMR spectra were in complete agreement with the α-glycosides and nOe experiments[10] further confirmed the structures assigned. Except *t*-BuOH, other alcohols such as benzyl alcohol, cyclohexanol and allyl alcohol reacted smoothly to give the corresponding C-2-methylene-*O*-glycosides **3a**, **3b**, **3c** and **3d** in fair to good yields (Table 1). A sugar derived alcohol **4** also reacted with **1** to yield the corresponding disaccharide **5** in 65% yield possessing α-configuration.

Because of the importance[11] of *O*-aryl glycosides we reacted phenols (phenol, *p*-cresol, β-naphthol) with **1** and **2** in the presence of Nafion-H as a catalyst. Although the parent phenol did not react to give any clean product, *p*-cresol and β-naphthol reacted smoothly with **2** to give the corresponding *O*-glycosylated products **6** and **7** in 60 and 65% yields, respectively, but interestingly having β-configurations. It is noteworthy that *O*-aryl glycosides were not formed when phenols were reacted with **1** and **2** using $BF_3{\cdot}Et_2O$ as a catalyst as reported by Ramesh and Balasubramanian.[12] Instead, glycosylation was found to take place using phenols and under Mitsunobu activation conditions to give a mixture of α and β-*O*-aryl glycosides and a small amount of aryl ether, via allylic substitution. In this regard the use of Nafion-H in the present study to form only β-*O*-aryl glycoside is useful.

☆ To be considered as Part 1 in the series: 'Transformations in Carbohydrate Chemistry'.

Keywords: montmorillonite K-10; Nafion-H; *O*- and *C*-glycosides.

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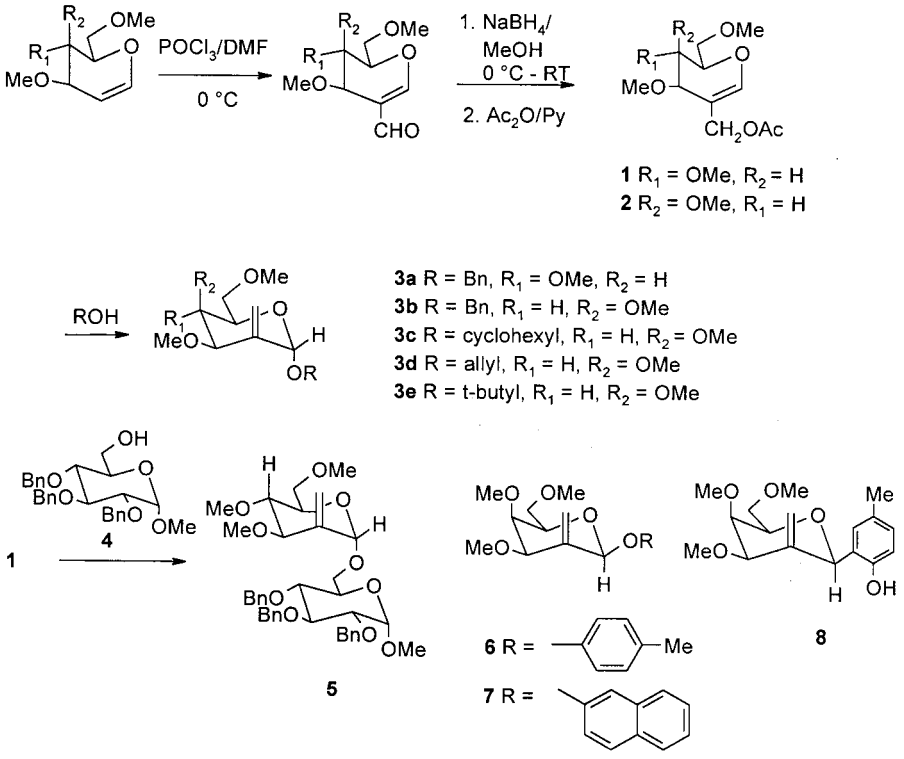
PII: S0040-4020(00)00775-4

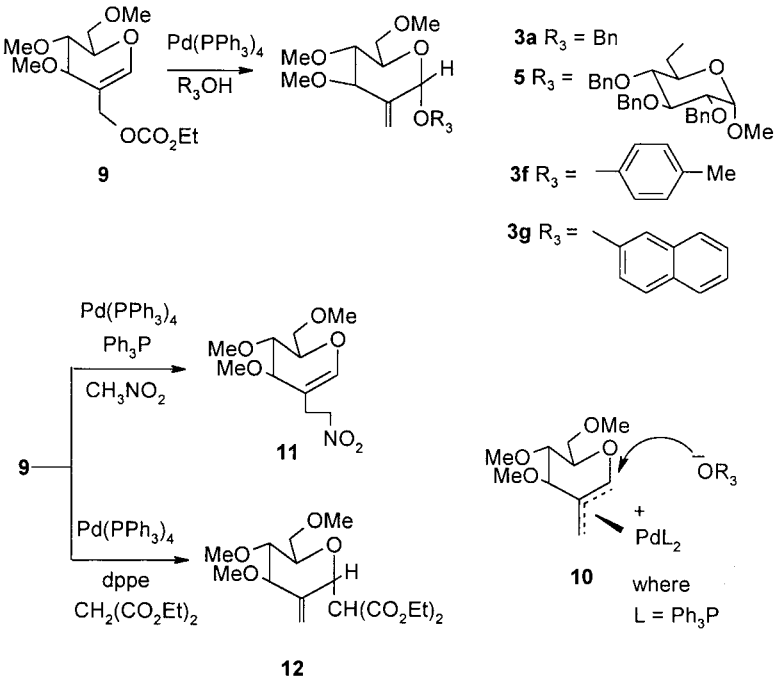


Scheme 1.

Since no glycosylation occurred with *t*-BuOH in the presence of Nafion-H as a catalyst, probably due to its strong acidic nature, we utilized a yet another solid catalyst viz. montmorillonite K-10[6] for this purpose which has, in recent times, gained importance in organic synthesis due to its stability, ease of handling, lack of corrosion and ease of regeneration. It has also been employed in carbohydrate chemistry, for example, in *O*-glycosylation[13] involving trichloroacetimidate donors, *C*-glycosylation of glycals[14] and unprotected sugars.[15] In the present study, gratifyingly, *t*-BuOH reacted smoothly with **2**, in the presence of montmorillonite K-10 (1 wt. equiv.) to form the corresponding *O*-glycoside **3e** in 70% yield. Interestingly and surprisingly this *O*-glycoside also possessed α-configuration as confirmed by nOe experiments. Likewise, several other glycosyl acceptors viz. benzyl alcohol, cyclohexanol, allyl alcohol, and sugar derived alcohol **4** reacted smoothly to form the corresponding *O*-glycosides in good yields (Table 1), having α-configurations. Results with *p*-cresol and β-naphthol, however, were rather unexpectedly different. Thus, with *p*-cresol, a *C*-glycoside **8** was formed possessing β-configuration whereas with β-naphthol, on the other hand, a β-*O*-glycoside **7** was obtained. Formation of *C*-glycoside **8** is not surprising as Toshima et al.[15] have

Table 1.

Entry	Allyl acetate	Nucleophile	Catalyst	Time (h)	Product	Yield (%)	Rotation $[\alpha]_D$ in CH_2Cl_2, Cl
1	**1**	BnOH	Nafion H	20	**3a**	80	+116.4
2	**2**	BnOH	Montmorillonite	15	**3b**	70	+122.6
3	**2**	BnOH	$LiClO_4$	1	**3b**	75	+100.5
4	**1**	**4**	Nafion H	15	**5**	65	+98.1
5	**1**	**4**	Montmorillonite	12	**5**	65	+90.1
6	**1**	**4**	$LiClO_4$	2	**5**	75	+100.2
7	**2**	Cyclohexanol	Nafion-H	10	**3c**	70	+80.0
8	**2**	Cyclohexanol	Montmorillonite	8	**3c**	65	+82.0
9	**2**	Cyclohexanol	$LiClO_4$	1.5	**3c**	65	+75.4
10	**2**	Allyl alcohol	Nafion H	6	**3d**	65	+74.6
11	**2**	Allyl alcohol	Montmorillonite	4	**3d**	70	+78.0
12	**2**	Allyl alcohol	$LiClO_4$	1	**3d**	75	+80.9
13	**2**	*t*-BuOH	Nafion-H	–	–	–	
14	**2**	*t*-BuOH	Montmorillonite	5	**3e**	70	+70.0
15	**2**	*t*-BuOH	$LiClO_4$	1	**3e**	75	+64.0
16	**2**	*p*-cresol	Nafion-H	4	**6**	60	−294.0
17	**2**	*p*-cresol	Montmorillonite	5	**8**	62	−60.2
18	**2**	*p*-cresol	$LiClO_4$	4	**6**	65	−270
19	**2**	β-naphthol	Montmorillonite	5	**7**	60	−288.0
20	**2**	β-naphthol	$LiClO_4$	1	**7**	70	−280.9
21	**2**	β-naphthol	Nafion-H	7	**7**	65	−288.0

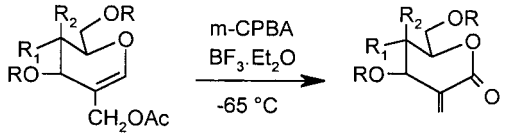


Scheme 2.

reported β-aryl-*C*-glycosylations with unprotected sugars with phenols in the presence of montmorillonite K-10. However, formation of **7** is not clear.

Ever since the introduction of $LiClO_4$ in organic solvents by Grieco et al.[7a] it has gained enormous importance organic synthesis. In carbohydrate chemistry, Waldman et al.[16] have made use of $LiClO_4$ for glycosylation under neutral conditions. In our case, we have found that **2** underwent smooth glycosylation with a variety of alcohols, including *t*-BuOH using a 0.07 M solution of $LiClO_4$ in CH_2Cl_2 and the corresponding α-*O*-glycosides were obtained in good yields in 1–1.5 h at 0°C to room temperature (Table 1). On the other hand, phenols such as *p*-cresol and β-naphthol gave the corresponding β-*O*-glycosides as observed in Nafion-H mediated reactions (vide supra). In general, it was noted that reactions with $LiClO_4$ were more clean than with Nafion-H or montmorillonite K-10. Since the use of acid catalysts led to the formation of α-glycosides in all the cases using aliphatic alcohols as glycosyl acceptors, we decided to explore palladium catalyzed reactions for *O*-glycosylations hoping to exploit the orientation of π-allyl palladium complex to direct the stereoselectivity.

Initial experiments with allyl acetate **1** with benzyl alcohol as a nucleophile in the presence of $Pd(Ph_3)_4$ led to no reaction. However, use of the allylic carbonate **9** (Scheme 2) in such a reaction led to the formation of the α-glycoside **3a** in 65% yield in refluxing THF with $Pd(PPh_3)_4$. Likewise, **4** also readily reacted with **9** to form **5**. Since these glycosides were 'α' in nature, it is clear that the formation of the π-allyl complex **10** (Scheme 2) occurs from β-face followed by the attack of nucleophiles from 'α' side. This became even more clear when *p*-cresol and β-naphthol were found to give the corresponding α and not β-glycosides **3f** and **3g**. Clearly, these results with phenols are complementary to the ones obtained using Nafion-H, montmorillonite K-10 and $LiClO_4$ where β-glycosides were formed. The geometry of the α-glycoside bond was confirmed by nOe experiments. In an effort to study the scope of these palladium catalyzed reactions some carbon nucleophiles were also utilized to form *C*-glycosides. Towards this effect nitromethane and diethyl malonate were reacted with **1**. Unfortunately, reaction of nitromethane with **9** in the presence of $Pd(PPh_3)_4$ gave the corresponding allylated product **11** (Scheme 2) and not the expected glycosylated product. On the other hand, diethyl malonate did not react at all under these



1 R_1 = OMe , R_2 = H
2 R_1 = H, R_2 = OMe
13 R_1 = OBn, R_2 = H[12]
14 R_1 = H, R_2 = OBn[12]

Yield
15a R = R_1= OMe, R_2 = H (65%)
15b R = R_2 = OMe, R_1 = H (62%)
15c R = R_1 = OBn, R_2 = H (76%)[17]
15d R = R_2 = OBn, R_1 = H (78%)[17]

Scheme 3.

conditions. However, use of dppe as a ligand, in place of Ph_3P, led to the formation of the expected *C*-glycoside **12** having α-configuration.

In continuation to explore the potential of compounds **1** and **2**, we have found that they can be easily converted into a α-methylene δ-valerolactones such as **15** (Scheme 3). Importance of these kinds of lactones has been demonstrated by Giese and Schmidt[2] in their studies pertaining to *C*-disaccharide synthesis via radical mediated conjugate addition of an anomeric pyranosyl radical. There have been three reports on the synthesis of such lactones, by (i) Schmidt et al.[17] using sulfur chemistry, (ii) by Ramana and Nagarajan[18] using cyclopropane based chemistry and more recently, (iii) by Chmielewski et al.[19] using compounds of type **1** and **2** (Scheme 3) in three steps in moderate yields. We have, however, found that compounds **1** and **2** (and their benzyl derivatives) react with *m*-chloroperbenzoic acid[20] in the presence of $BF_3{\cdot}Et_2O$ to directly give the corresponding α-methylene-δ-valerolactones in good yields (cf. Experimental). In view of the importance of such lactones in C-disaccharide synthesis[2] and their being potentially useful synthons, due to α,β-unsaturated lactone moiety and the fact that compounds of type **1** and **2** are readily available from the corresponding glycals, we believe that the synthesis described here will find application.

In summary, our study related to the employment of substrates like **1** and **2** (or their derivatives) has led to the formation of *O*- and *C*-glycosides (including aryl glycosides) in highly stereoselective manner. Further these substrates are also useful in the synthesis of α-methylene-δ-valerolactones, which are useful intermediates.

Experimental

Optical rotations were recorded on Autopol II automatic polarimeter at the wavelength of the sodium D-line (589 nm) and at an ambient temperature. Infrared spectra were recorded on Perkin–Elmer 1320 or Bruker FT/IR Vector 22 spectrometers. ^{1}H NMR spectra were recorded on Jeol-PMX 60, Bruker WP-80, Bruker WM-300 (or 400) or Jeol LA-400 NMR spectrometers using tetramethylsilane as the internal standard. ^{13}C NMR spectra were recorded on Bruker WM-300 and 400 or Jeol LA-400 NMR spectrometers. FAB mass spectra were obtained using Jeol SX 102/DA-6000 spectrometer. Elemental analyses were carried out in Coleman automatic C,H,N,O or Carlo–Erba EA 1110 analyzer.

Nafion® resin (Dupont) was obtained as a gift from Prof. George Olah and Prof. G. K. Surya Prakash, University of Southern California, USA. The Nafion resin, obtained in the form of Nafion-K, was converted to Nafion-H as per the reported procedure.[5a] Montmorillonite (K-10) was obtained from Fluka Chemical Company, Switzerland. Lithium perchlorate was prepared[7a] by acidfying an aqueous solution of LiOH with perchloric acid (70%).[7b] The resulting solid was dried at 150°C under vacuum for 10 h to obtain anhydrous $LiClO_4$. 3,4,6-Tri-*O*-methyl-C-2-formyl-glycals and 3,4,6-tri-*O*-benzyl-C-2-formyl glycals were prepared according to the literature report.[3]

Preparation of allyl actates 1 and 2

To a solution of a C-2-formyl glycal (1.96 g, 9.1 mmol) and dry MeOH (60 mL) at 0°C, sodium borohydride (504 mg, 13.6 mmol) was added portionwise over a period of 15 min. The reaction mixture was brought to room temperature and stirred for 5–10 min before quenching with a saturated solution of NH_4Cl (1–2 mL). Methanol was evaporated under reduced pressure and the product extracted with CH_2Cl_2 (3×40 mL) and washed with water (2×25 mL) followed by brine (25 mL). The dried (anhydrous Na_2SO_4) organic phase was concentrated on rotary evaporator and the crude product purified by column chromatography.

1,5-Anhydro-3,4,6-tri-*O*-methyl-1,2-di-deoxy-2-acetoxy-D-arabino-hex-1-enitol (1). Yield: 90%. $[\alpha]_D$=+102 (*c* 1, CH_2Cl_2). IR (CCl_4): ν 1720 cm^{-1}. ^{1}H NMR ($CDCl_3$, 80 MHz): δ 2.0 (s, 3H, –OCO*CH*$_3$), 3.46 (s, 3H, –CH_2O*CH*$_3$), 3.46–3.75 (m, 9H, 2×–OCH$_3$, $H_{6,6'}$, H_4), 3.83–3.85 (d, 1H, J=5 Hz, H_3), 4.08–4.15 (m, 1H, H_5), 4.44–4.66 (q, 2H, J=12.8 Hz, –*CH*$_2$OAc), 6.52 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.92, 57.52, 58.55, 58.97, 62.19, 70.17, 74.94, 75.09, 75.66, 108.02, 145.13, 170.86. Mass spectrum (*m*/*z*): 283 [(M^++23), 100], 201 [(M^+−60), 32], 171(9). Anal. Calcd for $C_{12}H_{20}O_6$ C, 55.37; H, 7.74. Found: C, 55.62; H, 8.17.

1,5-Anhydro-3,4,6-tri-*O*-methyl-1,2-di-deoxy-2-acetoxy-methyl-D-lyxo-hex-1-enitol (2). Yield: 84%. $[\alpha]_D$=+84 (*c* 1, CH_2Cl_2). IR (CCl_4): ν 1720 cm^{-1}. ^{1}H NMR ($CDCl_3$, 80 MHz): δ 2.0 (s, 3H, –OCO*CH*$_3$), 3.41 (s, 3H, –O*CH*$_3$), 3.51–3.58 (s, 6H, 2×–O*CH*$_3$), 3.63 (dd, 2H, J=7.2 Hz, 5.4 Hz, $H_{6,6'}$), 3.76 (m, 1H, H_4), 3.97 (d, 1H, J=3.6 Hz, H_3), 4.17–4.19 (m, 1H, H_5), 4.41–4.73 (q, 2H, J=12.7 Hz, –*CH*$_2$OAc), 6.47 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.97, 57.44, 59.09, 59.89, 62.33, 70.23, 73.24, 75.30, 75.46, 108.26, 144.67, 170.84. Mass spectrum (*m*/*z*): 283 [(M^++23), 100], 201 [(M^+−23), 20], 171(9). Anal. Calcd for: $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.10; H, 8.00.

General procedure for the glycosylation of allyl acetates 1 and 2 using Nafion-H

To a solution of allyl acetates **1** or **2** (1 mmol) at 0°C, in dry CH_2Cl_2 (2 mL), Nafion-H (wt. equiv.) and glycosyl acceptor (1.1 mmol) were added. After stirring for 12 h at room temperature, it was filtered over a sintered funnel. The reaction was monitored by TLC (H_2SO_4 charring). The filtrate was evaporated to dryness and was purified by column chromatography.

General procedure for the glycosylation of allyl acetates 1 and 2 using montmorillonite K-10

To a solution of allylic acetate **1** and **2** (1 mmol) at 0°C, in dry CH_2Cl_2 (2 mL) and montmorillonite (1 wt. equiv.) and a glycosyl acceptor (1.1 mmol) was added and stirred under nitrogen atmosphere for the time specified in Table 1. After the completion of the reaction, (tlc monitoring) the reaction mixture was filtered through a sintered funnel and the solvent evaporated at reduced pressure to give a crude product, which was purified by column chromatography.

General procedure for glycosylation of allyl acetate 1 and 2 using 0.07 M $LiClO_4$ in dichloromethane

Anhydrous $LiClO_4$ (40 mg, 0.38 mmol) was dissolved in 4 mL of dry CH_2Cl_2 under N_2 atmosphere and to this was added a mixture of allyl acetate **1** or **2** (50 mg, 0.19 mmol) and a glycosyl acceptor (0.19 mmol) in 1.4 mL of CH_2Cl_2, dropwise at 0°C. The reaction was stirred at room temperature for the specified time. After the reaction was complete, reaction mixture was washed with H_2O (2×10 mL) and subsequently with CH_2Cl_2 (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography.

Benzyl-3,4,6-tri-*O*-methyl-2-deoxy-*C*-2-methylene-α-D-xylo-hexopyranoside (3a). $[\alpha]_D$=+116.4 (*c* 1, CH_2Cl_2). IR (CCl_4): ν 1605 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.19 (t, 1H, *J*=9.8 Hz, H_4), 3.41 (s, 3H, OCH_3), 3.53–3.79 (m, 8H, 2×OCH_3, $H_{6,6'}$), 3.21–3.86 (m, 1H, H_5), 4.04–4.08 (m, 1H, H_3), 4.5–4.74 (ABQ, 2H, *J*=11.4 Hz, CH_2OPh), 5.07 (s, 1H, olefinic-*H*), 5.18 (s, 1H, olefinic-*H*), 5.19 (s, 1H, H_1). 7.31 (s, 5H, Ph-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 59.2, 59.3, 60.4, 68.8, 71.3, 71.5, 81.7, 82.7, 100.7, 110.5, 127.6, 127.9, 128.3, 137.5, 142.1. Mass spectrum (*m*/*z*): 200 (M^+-108), 142, 91. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.17; H, 7.58.

Benzyl-3,4,6-tri-*O*-methyl-2-deoxy-*C*-2-methylene-α-D-lyxo-hexopyranoside (3b). $[\alpha]_D$=+122.6 (*c* 1.3, $CHCl_3$). IR (CCl_4): ν 1610 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.40 (s, 3H, –$CH_2O$$CH_3$), 3.49 (s, 3H, –O$CH_3$), 3.54 (s, 3H, –O$CH_3$), 3.49–3.61 (m, 2H, $H_{6,6'}$), 3.72 (br s, 1H, H_4), 4.10–4.16 (br s and t, 2H, H_3, H_5, $J_{5,6\ 6'}$=8 Hz), 4.52–4.79 (ABQ, 2H, CH_2OPh, J_{gem}=14.7 Hz), 5.18 (s, 1H, olefinic-*H*), 5.28 (s, 1H, olefinic-*H*), 5.23 (s, 1H, H_1), 7.31 (s, 5H, Ph-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 59.8, 60.1, 60.7, 69.9, 71.8, 71.9, 82.0, 82.9, 101.0, 111.2, 127.8, 127.9, 128.3, 137.6, 142.3. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.52; H, 7.58.

Methyl-6-*O*-(3,4,6-tri-*O*-methyl-*C*-2-methylene-α-D-xylo-hexopyranosyl)-2,3,4,tri-*O*-benzyl-α-D-glucopyranoside (5). $[\alpha]_D$=+76.7 (*c* 1.7, CH_2Cl_2); IR (CCl_4): ν 1608 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.16–3.5 (t, 1H, *J*=10.4 Hz, H_4), 3.34 (s, 3H, –OCH_3), 3.37 (s, 3H, –OCH_3), 3.45–3.52 (m, 2H, $H_{3'}$, $H_{5'}$, $H_{6,6'}$), 3.52–3.56 (s, 8H, 2×–OCH_3, $H_{6,6'}$), 3.67–3.85 (m, 4H, $H_{2'}$, H_5, $H_{6,6'}$), 3.9–4.04 (m, 2H, H_3, $H_{4'}$), 4.59–5.0 (dd, 6H, 3×OCH_2Ph), 4.6 (d, 1H, J_{1-2}=3.5 Hz, $H_{1'}$), 5.05 (s, 1H, olefinic-*H*), 5.14 (s, 1H, olefinic-*H*), 5.15 (s, 1H, H_1), 7.29 (s, 15H, 3×Ph-*H*). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.9, 54.0, 54.1, 55.2, 60.6, 64.7, 66.1, 66.2, 68.2, 69.7, 70.6, 71.5, 71.9, 72.3, 72.7, 74.9, 92.7, 96.3, 105.4, 122.5, 122.7, 122.9, 123.2, 123.3, 133.0, 133.2, 133.5, 136.8. Mass spectrum (*m*/*z*): No M+1 peak, 201, 171. Anal. Calcd for $C_{38}H_{48}O_{10}$: C, 68.67; H, 7.28. Found: C, 68.79; H, 7.24.

Cyclohexanyl-3,4,6-tri-*O*-methyl-2-deoxy-*C*-2-methylene-α-D-lyxo hexopyranoside (3c). $[\alpha]_D$=+98.18 (*c* 1.1, $CHCl_3$); IR (CCl_4): ν 1610 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.26–1.91 (m, 11H, cyclohexyl protons), 3.40 (s, 3H, $CH_2O$$CH_3$), 3.49 (s, 3H, 2×O$CH_3$), 3.54 (s, 3H, –O$CH_3$), 3.54–3.62 (m, 2H, $H_{6,6'}$), 3.72 (br d, 1H, H_4), 4.11–4.13 (m, 2H, H_3, H_5), 5.14 (s, 1H, olefinic-*H*), 5.22 (s, 1H, olefinic-*H*), 5.27 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 26.0, 25.5, 29.0, 31.5, 33.4, 57.3, 59.1, 60.9, 69.9, 70.3, 70.8, 78.6, 79.3, 100.8, 110.8, 141.2. Mass spectrum (*m*/*z*): No M+1 peak, 201 (M^+-99], 169, 170, 139. Anal. Calcd for $C_{16}H_{28}O_5$: C, 64.00; 9.40. Found: C, 63.90; H, 9.46.

Allyl-3,4,6-tri-*O*-methyl-2-deoxy-2-methylene-α-D-lyxo-hexopyranoside (3d). $[\alpha]_D$=+74.6 (*c* 1.5, $CHCl_3$); IR (CH_2Cl_2): ν 1615 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.40 (s, 3H, $CH_2O$$CH_3$), 3.50 (s, 3H, O$CH_3$), 3.54 (s, 3H, O$CH_3$), 3.52–3.71 (m, 2H, $H_{6,6'}$), 3.72 (br d, 1H, *J*=3.5 Hz, H_4). 4.00–4.21 (m, 4H, H_5, H_3, allylic-CH_2), 5.18–5.21 (3×s, 3H, 2×olefinic-*H*, H_1), 5.27 (s, 1H, $H_{olefinic}$), 5.33 (s, 1H, $H_{olefinic}$), 5.86–5.99 (m, 1H, vinylic-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 59.1, 59.2, 60.4, 71.2, 76.4, 79.6, 81.6, 82.6, 100.4, 110.3, 117.3, 133.8, 142.0. Mass spectrum (*m*/*z*): No M^+ or $[M+1]^+$ peak; 201 (M^+-45], 170, 139. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.46; H, 8.59. Found: C, 60.45; H, 8.56.

***t*-Butyl-1,5-anhydro-3,4,6-tri-*O*-methyl-2-methylene-α-D-lyxo-hexopyranoside (3e).** $[\alpha]_D$=+64 (*c* 0.5, $CHCl_3$); IR (CH_2Cl_2): ν 1615 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.25 (s, 9H, *t*-butyl-*H*), 3.39 (s, 3H, –$CH_2O$$CH_3$), 3.49 (s, 3H, O$CH_3$), 3.54 (s, 3H, OCH_3), 3.54–3.60 (m, 2H, $H_{6,6'}$), 3.73 (br d, 1H, $J_{3,4}$=2.5 Hz H_4), 4.13 (d, 1H, $J_{5,6}$=2.5 Hz, H_3), 4.18 (t, 1H, $J_{5,\ 6,6'}$=7.3 Hz H_5), 5.05 (s, 1H, olefinic-*H*), 5.19 (s, 1H, olefinic-*H*), 5.40 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 33.8, 56.6, 59.7, 60.2, 60.6, 65.8, 71.8, 71.9, 72.5, 82.5, 82.9, 100.3, 110.9, 141.3. Mass spectrum (*m*/*z*): No $M+1/M^+$ peak, 201 (M^+-73], 169, 156. Anal. Calcd for $C_{14}H_{26}O_5$: C, 61.31; H, 9.56,. Found: C, 61.30; H, 9.60.

4-Methyl-2-*O*-(3,4,6-tri-*O*-methyl-2-methylene-β-D-lyxo-hexopyranosyl)-phenol (6). $[\alpha]_D$=−294.0 (*c* 1, $CHCl_3$), IR (CH_2Cl_2): ν 1610 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.48 (s, 3H, CH_3), 3.43 (s, 3H, OCH_3), 3.44 (s, 6H, 2×OCH_3), 3.61–3.64 (m, 1H, H_4), 3.69–3.71 (m, 3H, $H_{6,6'}$, H_3), 4.18 (m, 1H, H_5), 5.58 (s, 1H, H_1), 6.18 (s, 1H, olefinic-*H*), 6.19 (s, 1H, olefinic-*H*), 6.90 (d, 2H, Ph-*H*), 7.00 (d, 2H, Ph-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.1, 56.8, 59.8, 69.6, 71.4, 71.4, 80.8, 81.0, 93.3, 111.0, 117.0, 119.2, 120.5, 129.3, 128.91, 135.1, 151.3. Mass spectrum (*m*/*z*): no $(M+1)^+$, 201 (M^+-107), 156. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.23; H, 7.85. Found: C, 66.30; H, 7.88.

1-*O*-(3,4,6-Tri-*O*-methyl-2-methylene-β-D-lyxo-hexopyranosyl)-naphthol (7). $[\alpha]_D$=−288.0 (*c* 1.5, $CHCl_3$). IR (CH_2Cl_2): ν 1615 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 3.47 (s, 9H, 3×OCH_3), 3.68 (d, 1H, *J*=4.2 Hz, H_4), 3.76–3.79 (m, 2H, $H_{6,6'}$) 3.96 (br s, 1H, H_3), 4.22–4.26 (m, 1H, H_5), 5.69 (s, 1H, H_1), 6.30 (s, 1H, olefinic-*H*), 6.31 (s, 1H, olefinic-*H*), 7.15–7.84 (m, 7H, naphthyl-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.87, 59.32, 59.54, 69.68, 71.54, 71.75, 80.85, 80.92, 93.47, 112.68, 119.02, 121.77, 123.73, 126.66, 128.39, 128.50, 129.20, 132.15, 135.04, 151.19. Mass spectrum (*m*/*z*): 345 $[M+1]^+$, 330, 300. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.76; H, 7.03. Found: C, 69.75; H, 7.00.

4-Methyl-2-(3,4,6-tri-*O*-methyl-2-methylene-β-D-lyxo-hexopyranosyl)-phenol (8). $[\alpha]_D=-60.2$ [*c* 0.8, $CHCl_3$], IR ($CDCl_3$): ν 3600 cm^{-1}, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.24 (s, 3H, CH_3), 3.34 (s, 3H, $-OCH_3$), 3.31–3.43 (s, 6H, 2×$-OCH_3$), 3.52 (dd, *J*=8 Hz, 2H, $H_{6,6'}$), 3.79 (br s, 1H, H_4), 4.05 (t, 1H, *J*=6 Hz, H_5), 4.11 (d, 1H, *J*=21 Hz, H_3), 5.04 (s, 1H, H_1), 5.21 (s, 1H, olefinic-*H*), 5.28 (s, 1H, olefinic-*H*), 6.29 (s, 1H, *OH*), 6.82–7.01, (m, 3H, Ar-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.9, 57.9, 59.10, 61.0, 69.5, 71.5, 73.2, 74.5, 78.3, 110.7, 117.0, 124.2, 125.9, 127.7, 129.9, 140.9, 150.9. Mass spectrum (*m/z*): 308 (M^+), 201, 156. Anal. Calcd for $C_{17}H_{24}O_6$: C, 66.23; H, 7.85, Found: C, 66.39; H, 7.75.

Preparation[21] of methyl-1,5-anhydro-3,4,6-tri-*O*-methyl-1,2-di-deoxy-D-arabino-hex-1-enitolyl-ethyl carbonate (9). To a stirred solution of allylic alcohol (100 mg, 0.45 mmol) in THF (2 mL), pyridine (181 mg, 2.26 mmol), ethyl chloroformate (245 mg, 2.20 mL) and catalytic amount of DMAP were added. The progress of the reaction was monitored by TLC. After completion of the reaction, (12 h) THF was evaporated under reduced pressure and the usual work up gave a crude product which was purified by flash column chromatography.

Yield: 65%. $[\alpha]_D=+100.9$ (*c* 1.5, $CHCl_3$). IR ($CDCl_3$): ν 1750 cm^{-1} ^1H NMR ($CDCl_3$, 300 MHz): δ 1.30 (t, 3H, *J*=7.35 Hz, OCH_2CH_3), 3.4 (s, 3H, OCH_3), 3.49 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.59–3.68 (m, 3H, H_4, $H_{6,6'}$), 3.89 (d, *J*=6 Hz, 1H, H_3), 4.07–4.12 (m, 1H, H_5), 4.20 (q, *J*=4.2 Hz, 2H, OCH_2CH_3), 4.5–4.7 (ABQ; 2H, *J*=8.2 Hz, CH_2-), 6.64 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 100 MHz); δ 15.0, 59.18, 59.4, 60.4, 60.5, 62.5, 71.3, 71.7, 82.0, 82.7, 110.1, 142.3, 165.5. Mass spectrum (*m/z*): No M^+ or $(M+1)^+$ peak, 201, 170.9, 138.9, 108.9. Anal. Calcd for $C_{13}H_{22}O_7$: C, 53.79; H, 7.64. Found: C, 54.01; H, 7.64.

General procedure for the Pd(0) catalyzed *O*- and *C*-glycosylations

To a solution of the carbonate **9** (1 mmol) in THF (2 mL), an alcohol or diethyl malonate or nitromethane (1 mmol) under N_2 atm, triphenylphosphine or dppe (10 mol%) and freshly prepared Pd(0) (2 mol%) were successively added. After refluxing for the given time, (for compounds **3a** and **5** the reaction time were, 8 and 10 h, respectively) the THF was evaporated, mixture was filtered over a sintered funnel and washed thoroughly with ethyl acetate (2×25 mL). The solvent was evaporated under reduced pressure and the crude product so obtained was purified by column chromatography.

***p*-Methyl phenyl-3,4,6-tri-*O*-methyl-*C*-2-methylene-α-D-arabino-hexo-pyranoside (3f).** $[\alpha]_D=+119.2$ (*c* 1.3, $CHCl_3$). IR (CH_2Cl_2): ν 1608 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.28 (s, 3H, CH_3), 3.36 (s, 3H, OCH_3), 3.39 (t, 1H, *J*=10 Hz, H_4), 3.57–3.62 (2s, 6H, 2×OCH_3), 3.47–3.62 (m, 2H, $H_{6,6'}$), 3.85–3.89 (m, 1H, H_5), 4.20 (d, 1H, *J*=12 Hz, H_3), 5.17 (s, 1H, olefinic-*H*), 5.26 (s, 1H, olefinic-*H*), 5.77 (s, 1H, H_1), 7.05 (q, *J*=9.3 Hz, Ph-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.2, 59.05, 59.8, 60.56, 70.71, 71.5, 77.8, 80.1, 100.1, 110.91, 117.09, 119.20, 120.57, 128.31, 130.47, 140.92, 151.33. Mass spectrum (*m/z*): 309 $(M+1)^+$, 201, (M^+-108), 171. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.23; H, 7.85. Found: C, 66.20; H, 7.86.

1-*O*-(3,4,6-tri-*O*-methyl-2-methylene-α-D-arabino-hexo-pyranoside)-2-naphthol (3g). $[\alpha]_D=+76.8$ (*c* 1.6, $CHCl_3$). IR (CH_2Cl_2): ν 1615 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.39 (s, 3H, OCH_3), 3.37–3.43 (m, 1H, H_4), 3.52–3.64 (m, 2H, $H_{6,6'}$), 3.61 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.90–3.95 (m, 1H, H_5), 4.28 (d, $J_{3,4}$=10.4 Hz, 1H, H_3), 5.34 (s, 1H, olefinic-*H*), 5.35 (s, 1H, olefinic-*H*), 6.00 (s, 1H, H_1), 7.16–7.80 (m, 7H, naphthyl-*H*). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 59.09, 60.48, 70.72, 71.98, 81.10, 82.06, 99.85, 110.62, 118.97, 124.117, 126.232, 127.103, 127.10, 127.53, 127.57, 129.31, 129.50, 134.31, 141.19, 154.05. Mass spectrum (*m/z*): 345 $(M+1)^+$, 201, 170, 139. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.76; H, 7.03. Found: C, 69.70; H, 7.00.

1,5-Anhydro-3,4,6-tri-*O*-methyl-1,2-di-deoxy-2-nitro-ethane-D-arabino-hex-1-enitol (11). Reaction time: 8 h. $[\alpha]_D=+120$ [*c* 0.7, $CHCl_3$). IR ($CDCl_3$): ν 1560 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.53–2.78 (m, 2H, $CH_2-CH_2NO_2$), 3.39 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.51 (s, 3H, OCH_3), 3.57–3.62 (m, 2H, CH_2OCH_3), 3.62–3.67 (m, 1H, H_4), 3.76 (d, 1H, *J*=8 Hz, H_3), 4.02–4.07 (m, 1H, H_5), 4.42–4.52 (m, 2H, CH_2NO_2), 6.29 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.05, 56.99, 58.65, 59.15, 70.07, 71.30, 71.5, 81.22, 82.60, 106.67, 142.87. Mass spectrum (*m/z*): 261 (M^+), 230, 201, 170. Anal. Calcd for $C_{11}H_{19}NO_6$: C, 50.57; H, 7.33; N, 5.36. Found: C, 50.56; H, 7.32; N, 5.35.

Ethyl-2-(1,5-anhydro-3,4,6-tri-*O*-methyl-1,2-di-deoxy-C-2-α-D-arabino-hexopyranosyl)-2-(ethoxy carbonyl) acetate (12). Reaction time: 5 h, $[\alpha]_D=+52.2$ [*c* 1, $CHCl_3$]. IR ($CDCl_3$): ν 1750 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz); δ 1.23–1.3 (m, 3H, *J*=6 Hz, OCH_2CH_3), 3.17–3.21 (d, *J*=10 Hz, 1H, H_4), 3.35 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.52–3.62 (m, 2H, $H_{6,6'}$), 3.66–3.69 (m, 1H, H_5), 3.86, 3.96 (m, 1H, H_3), 3.96–3.98 (d, 1H, *J*=12 Hz, $CH(CO_2Et)_2$), 4.11–4.26 (m, 4H, 2×OCH_2), 4.99 (d, 1H, *J*=12 Hz, H_1), 5.13 (s, 1H, olefinic-*H*), 5.23 (s, 1H,olefinic-*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.98, 53.58, 59.13, 59.21, 60.25, 61.56, 61.66, 71.22, 74.09, 81.23, 81.69, 86.07, 107.80, 140.80, 165.30. Mass spectrum (*m/z*): 329 $[M^+-31]$, 201 $[M^+-159]$, 171, 139. Anal. Calcd for $C_{17}H_{28}O_8$: C, 56.66; H, 7.83. Found: C, 56.66; H, 7.84.

Conversion of allyl acetates 1, 2, 13[12], and 14[12] to lactones 15a–15d respectively

General procedure. To a stirred solution of an allyl acetate, (1 mmol) in dry CH_2Cl_2 (5 mL), cooled to −65°C, was added *m*-CPBA (50%, 344 mg, 2 mmol) followed by dropwise addition of freshly distilled (from CaH_2) $BF_3{\cdot}Et_2O$ (0.12 mL, 1 mmol) under N_2 atmosphere. The reaction was stirred for about 1 h until it was complete (TLC monitoring) and then quenched with 2 mL of 10% aq. $Na_2S_2O_4$ solution and brought it to room temperature. Usual work up thereafter followed by column chromatography purification gave the desired lactones. Lactones **15c** and **15d** gave satisfactory spectral and analytical data which were comparable with the literature[17] values.

3,4,6-Tri-*O*-methyl-2-deoxy-2-methylene-D-arabino-hexono-1,5-lactone 3 (15a). Yield: 65%. $[\alpha]_D=-65$ [*c* 2, $CHCl_3$). IR (CCl_4): ν 1730 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.19 (t, 1H, *J*=8 Hz, H_4), 3.39, 3.52, 3.59 (3S, 3H each, 3×–OCH_3), 3.64–3.69, (m, 2H, 2×$H_{6,6'}$), 3.99 (br d, *J*=8.8 Hz, 1H, H_3), 4.26 (m, 1H, H_5), 5.96 (br s, 1H, olefinic-*H*), 6.6 (br s, 1H, olefinic-*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.7, 58.8, 59.3, 71.0, 77.2 78.6, 80.7, 130.1, 134.1, 164.8. Mass spectrum (*m/z*): 217 [$(M+1)^+$, 2.3], 216 [(M^+), 5.3], 201 (14.30), 139 (17), 46 (100). Anal. Calcd for C, 55.55; H, 7.46. Found: C, 55.50 H, 7.69.

3,4,6-Tri-*O*-methyl-2-deoxy-2-methylene-D-lyxo-hexono-1,5-lactone (15b). Yield: 62%. $[\alpha]_D=+80$ [*c* 1, $CHCl_3$). IR (CCl_4): 1730 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.42 (s, 3H, –OCH_3), 3.55, 3.57 (2s, 3H each, 2×–OCH_3), 3.59–3.71 (m, 2H, $H_{6,6'}$), 3.99 (br s, 1H, H_4), 4.11 (d, 1H, *J*=3.3 Hz, H_3), 4.4 (t, 1H, *J*=9.9 Hz, H_5), 6.11 (br s, 1H, olefinic-*H*), 6.64 (br s, 1H, olefinic-*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.4, 59.2, 60.4, 70.2, 71.7, 76.6, 80.0, 129.2, 133.8, 163.6. Mass spectrum (*m/z*): 216 [(M^+), 5], 201(3), 171 (10), 46 (100). Anal. Calcd for C, 55.55; H, 7.46. Found: C, 55.41; H, 7.42.

Acknowledgements

We are grateful to the Department of Science and Technology, New Delhi for financial support (through grant # SP/S1/G-07/1997). A. G. thanks UGC, New Delhi, for a Senior Research Fellowship.

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