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Mitsunobu Reaction of 1,5-Anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-hydroxymethyl-hex-1-enitols and 1,5-Anhydro-2-deoxy-4,6-O-protected-hex-1-enitols. A Novel Method for the Synthesis of 2-C-Methylene Glycosides and an Useful Alternative to Ferrier Rearrangement

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Abstract: A simple and convenient method for the synthesis of aryl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-hexopyranosides **5**,**6** and **7**, glycosides which are not accessible by the conventional Ferrier rearrangement, has been described based on the Mitsunobu reaction of alcohols **3** and **4** with substituted phenols. The anomeric configurations of glycosides **5** and **6** were established by detailed NOE studies. The reaction is also successfully extended to the synthesis of phthaloyl derivative **10**. A mild, neutral and non-acidic alternative to Ferrier rearrangement for the synthesis of 2,3-dideoxy-hex-2-enopyranosides has also been demonstrated with a variety of nucleophiles.

INTRODUCTION

The chemistry of unsaturated carbohydrates continues to receive wide attention owing to the importance of such compounds in the total synthesis of many natural products.[1] 2-Deoxy-2-C-substituted carbohydrates are important class of branched chain deoxy sugars and unsaturated nucleosides.[2] Particularly, the 2-C-methylene group is a key structural feature of molecules involved in the mechanism based inactivation of ribonucleotide diphosphate reductase.[3] Recently, a convenient synthesis of alkyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-hexopyranosides has been reported from our lab,[4] based on the acid catalysed rearrangement of a new Ferrier system *viz.*, 1,5-anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-acetoxymethyl-hex-1-enitols with various alcohols. However, this reaction could not be extended to the synthesis of the corresponding aryl glycosides **5**, **6** and **7**.[5] As a part of our research program on the investigation of the Mitsunobu reaction on various alcoholic systems and on our efforts towards the synthesis of unsaturated C-aryl glycosides, we examined the triphenyl phosphine - diethyl azodicarboylate (DEAD) mediated reaction on glycals **3** and **4**. In this paper, we report a facile synthesis of the aryl glycosides **5**, **6** and **7** based on the Mitsunobu reaction of alcohols **3** and **4** with substituted phenols. Alkyl-2,3-dideoxy-hex-2-enopyranosides serve as versatile intermediates for the synthesis of a variety of natural products.[1] Also, phenyl 2,3-dideoxy-hex-2-enopyranoside has been used as the starting material by Brakta *et al* [6] in their palladium(0) based approach to C-glycoside synthesis. The conventional method for the synthesis of 2,3-dideoxy-hex-2-enopyranosides is the Ferrier rearrangement which is invariably an acid catalysed reaction.[7] In the absence of acid catalysis, the rearrangement could be realised only at high temperatures and that too in the presence of a large excess of alcohols[8] or phenol.[6,9] Recently, Fraser-Reid and co-workers have reported an oxidative alternative to the Ferrier rearrangement.[10] The applicability of this reaction to a variety of nucleophiles has not been mentioned by the authors. Very recently, Toshima *et al* reported a novel and neutral method for the synthesis of alkyl-4,6-di-O-acetyl-2,3-dideoxy-hex-2-enopyranosides using DDQ, a powerful oxidant as a

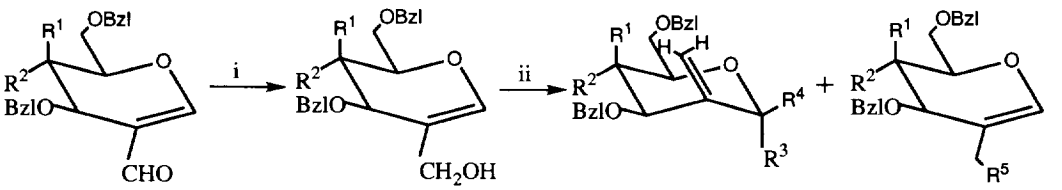
catalytic promotor.[11] However, this method suffers from the disadvantage that it cannot be applied to easily oxidisable nucleophiles such as phenols. In this paper, we also describe a neutral and mild route for the synthesis of 2,3-dideoxy-hex-2-enopyranosides by the Mitsunobu reaction of glycal **13** with different nucleophiles.

Results and Discussion

Mitsunobu reaction is one of the most convenient methods for the formation of ethers, esters, thioethers, lactams *etc.*[12] This reaction has been widely used in carbohydrates, particularly for the inversion of a secondary hydroxylic centre[10,13] and for the synthesis of glycosides.[14] Very few reports of allylic shifts under Mitsunobu conditions are also known.[15] In this paper, we report the Mitsunobu reaction of our recently disclosed allylic alcohol of sugars *viz.*, 1,5-anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-hydroxymethyl-hex-1-enitols **3** and **4**,[4] obtained by the reduction of the aldehydes **1** and **2**[16] respectively using liposoluble benzyltriethylammonium borohydride[17] (Scheme 1). The use of this liposoluble borohydride is found to increase the yield of the alcohol to 85% when compared to sodium borohydride (70%).[4] Treatment of the alcohol **3** with *p*-cresol in presence of Ph_3P and DEAD at room temperature afforded after column purification, a mixture of anomeric glycosides **5a** and **6a** as the major products with a minor amount of the aryl ether **8a** (Scheme 1; Entry 1; Table 1). The anomers **5a** and **6a** were separated by repeated recrystallisation . While the β-anomer **6a** crystallised , the α-anomer **5a** was obtained as a viscous liquid. Variation of the reaction conditions, temperature, mode of addition of the reagents *etc.* did not bring about any significant change either in the course of the reaction or in the distribution of the products. In all the modifications tried, the products were obtained more or less in the same ratio. The reaction was also found to proceed with equal feasiblity when *p*-methoxyphenol was used as a nucleophile (Scheme 1; Entry 2, Table 1).

The anomeric configurations of the glycosides **5** and **6** were confirmed by detailed ^1H NMR NOE studies. In the α-anomer **5a**, where the anomeric proton is equatorially oriented, the spatial proximity between $H\text{-}7_a$ and H-1 was found to be well within the range for NOE to be observed (Fig. 1). Thus irradiation of the signal due to the $H\text{-}7_a$was found to enhance the intensity of the signal due to H-1 by 16.8%. Also irradiation of the signal due to the anomeric proton enhanced the intensity of the signal due to $H\text{-}7_a$ by 7.7%. Further, since H-1 does not have 1,3-diaxial relationship with H-3 and H-5, no NOE were observed between them. The results of the NOE studies thus confirm that the anomeric configuration of **5a** is α.

Conversly, in the β-anomer **6a**, the anomeric proton has a *syn* 1,3-diaxial relationship with H-3 and H-5, whereas it is not spatially close to $H\text{-}7_a$ or $H\text{-}7_b$ (Fig. 1). Hence, one might expect that irradiation of the signal due to H-1 should result in the enhancement of intensity of the signals due to H-3 and H-5 and *vice versa*. Also, no enhancement could be expected in the intensity of the signals due to $H\text{-}7_a$ or $H\text{-}7_b$. Irradiation of the signal due to H-1 enhanced the intensities of the signals due to H-3 and H-5 by 7.7% and 9.1% respectively. Similarly the intensities of the signals due to H-1 and H-3 were enhanced by 8.7% and 6.2% respectively when the signal due to H-5 was irradiated. Also irradiation of signal due to H-3 resulted in the enhancement of the signal intensities of H-1 and H-5 by 8.6% and 10.2% respectively. The results of the NOE studies are in accordance with the expectation thus establishing the anomeric configuration of the glycoside **6a** is β. Further, the NOE studies also indicate that the β-anomer **6a** exists in the normal $^4C_1$ conformation as shown in Fig.1 in contrast



1 **3** **5, 6** **8**

2 **4** **7** **9**

10

Bzl = $PhCH_2$

1, 3, 5, 6, 8 = R^1 = H; R^2 = OBzl

2, 4, 7, 9, 10 = R^1 = OBzl; R^2 = H

5a, 7a = R^3 = *p*.Me-C_6H_4-O- ; R^4 = H

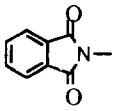
5b, 7b = R^3 = *p*.MeO-C_6H_4-O- ; R^4 = H

6a = R^3 = H; R^4 = *p*.Me-C_6H_4-O-

6b = R^3 = H; R^4 = *p*.MeO-C_6H_4-O-

8a, 9a = R^5 = *p*.Me-C_6H_4-O-

8b, 9b = R^5 = *p*.MeO-C_6H_4-O-

10 = R^3 =  ; R^4 = H

i. Benzyltriethylammonium borohydride, CH_2Cl_2, room temperature, 1d, 85%

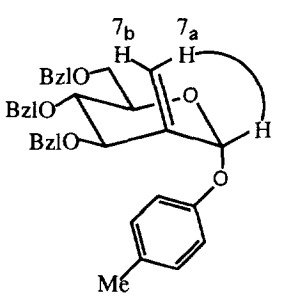
ii. Ph_3P, DEAD, benzene, room temperature

Scheme 1

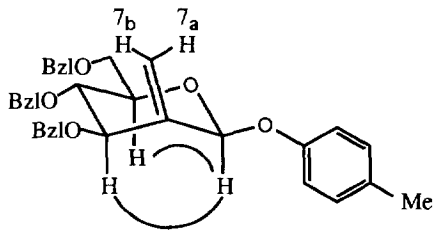
Table 1: Mitsunobu reaction of alcohols **3** and **4** with phenols and phthalimide

Entry	Alcohol	Product	Ratio[a]	Yield[b] (%)	Reaction time (h)
1	**3**	**5a+6a+8a**	40:40:20	85	10
2	**3**	**5b+6b+8b**	38:38:24	82	10
3	**4**	**7a+9a**	85:15	82	10
4	**4**	**7b+9b**	80:20	75	10
5	**4**	**10**	-	65	15

a = ratio based on the relative integral areas of the anomeric protons in the high resolution ^{1}H NMR spectra of the crude products
b = overall isolated yield after column purification



5a



6a

Fig 1

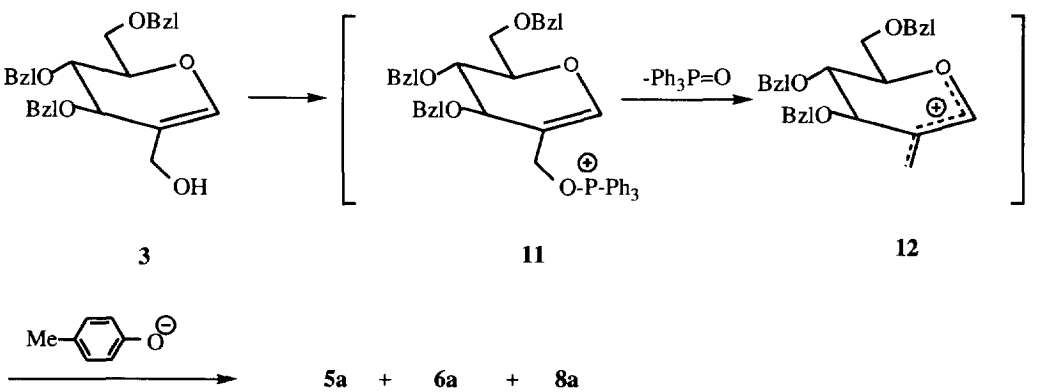
to aryl-4,6-di-O-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosides which prefer to exist in the inverted ^5H_O conformaton due to anomeric effect.[18,19] Thus, the present investigation also illustrates the utility of NOE studies to determine the anomeric configuration of such systems which is difficult to assign by other means.

The reaction was also successfully extended to the alcohol **4** (Scheme 1). Surprisingly, the Mitsunobu reaction of alcohol **4** with substituted phenols yielded stereoselectively only the α-glycosides **7** as the major product with minor amount of the aryl ether **9** (Scheme 1; Entries 3,4; Table 1). It should be mentioned here that the minor product aryl ether **9** was found to be unstable and decomposes when exposed to acidic reagents, even in $CDCl_3$. The stereochemistry at the anomeric centre of **7** was confirmed to be α by ^{1}H NMR NOE studies. In

the glycoside **7a**, irradiation of the signal due to H-1 (δ 5.90) was found to enhance the intensity of the signal due to H-7_a (δ 5.38) by 7.1%. Conversly, the signal due to H-1 was enhanced by 17.3% when the signal due to H-7_a was irradiated. The stereoselective formation of α-glycoside in this case indicates that the stereochemistry of the substituent at C-4 plays an important role in deciding the course of the reaction. The Ph_3P-DEAD mediated reaction of alcohol **4** with phthalimide as a nucleophile, interestingly afforded the phthaloyl derivative **10** as the only isolable product (Scheme 1; Entry 5; Table 1). The stereochemistry at the anomeric centre was confirmed to be α by the NOE studies as before.

The preferential attack of the nucleophiles at the anomeric centre (*i.e.* at the allylic end) in spite of the hydroxylic centre being a primary one is noteworthy.

Based on the products obtained, one could envisage an ionisation mechanism involving the intermediacy of highly stabilised allylic cation which is also an oxonium ion (Scheme 2).

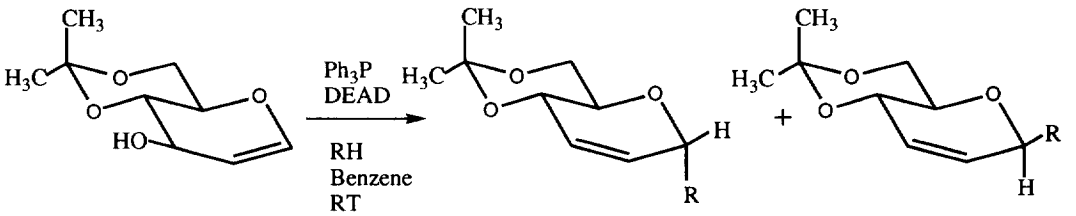


Scheme 2

Thus the methodology described above provides a convenient access to aryl-2-deoxy-2-methylene-hexopyranosides, compounds which cannot be prepared by the conventional Ferrier rearrangement.[5] Further, the successful preparation of **10** suggests that this method could also provide a convenient route for the synthesis of 2'C-methylene nucleosides.[2]

Guthrie *et al* in 1981,[20] reported that the Ph_3P-DEAD mediated reaction of 1,5-anhydro-4,6-O-benzylidene-2-deoxy-D-*arabino*-hex-1-enitol with benzoic acid afforded 1-O-benzoyl-4,6-O-benzylidene-2,3-dideoxy-α-D-*erythro*-hexo-2-enopyranose as the sole product. However, the synthetic utility of this reaction was not explored in detail by these authors. Very recently, Sobti *et al*[21] reported the synthesis of aryl glycosides by the Mitsunobu reaction of *glucal* , *rhamnal* and *fucal*. The authors have restricted their study to phenoxide nucleophiles and only two substituted phenols were tried. The importance of 2,3-dideoxy-hex-2-enopyranosides as key intermediates in many total synthesis[1] as well as the recent development of newer methods[10,11] for their synthesis prompted us to carry out a detailed investigation of the Mitsunobu reaction of glycal **13**. Treatment of

glucal **13**[22] with *p*-cresol in presence of Ph_3P and DEAD at room temperature in benzene, afforded after column purification, a mixture of anomeric glycosides **14a** and **15a** in the ratio 80 : 20. The anomers were separated by preparative HPLC and characterised thoroughly (Scheme 3; Entry 1; Table 2).



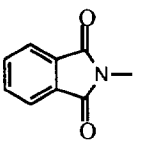
13 **14** **15**

14a, **15a** : R = *p*.Me-C_6H_4-O

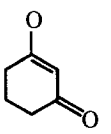
14b, **15b** : R = *p*.MeO-C_6H_4-O

14c, **15c** : R = AcO

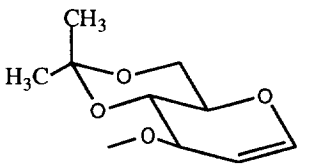
14d, **15d** : R =



14e, **15e** : R =



14f **15f** : R =



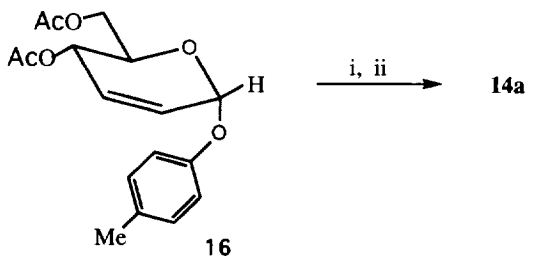
Scheme 3

Table 2 : Mitsunobu reaction of glycal **13** with various nucleophiles

Entry	Product	Ratio	Yield[a] (%)	Reaction time (h)
1	**14a + 15a**	80 : 20[b]	80	5
2	**14b + 15b**	85 : 15[b]	78	5
3	**14c + 15c**	90 : 10[c]	80	8
4	**14d + 15d**	65 : 35[d]	70	10
5	**14e + 15e**	70 : 30[c]	65	10
6	**14f + 15f**	90 : 10[c]	55	48

a = overall isolated yield of the anomeric mixtures after column purification
b = ratio based on HPLC analysis. anomers were separated and characterised
c = ratio based on the relative ratios of the integral areas of the anomeric protons of the α and β anomers
d = ratio based on the relative ratios of the integral areas due to H-3 of the α and β anomers

The anomeric configuration of aryl glycoside **14a** was confirmed to be α by comparing its spectral data and specific rotation with that of an authentic sample prepared as per scheme 4. Hydrolysis of (*p*-methyl)phenyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside **16**[18] (whose configuration at the anomeric centre was established as α) using Na_2CO_3 in MeOH followed by isopropylidenation with 2,2-dimethoxypropane in presence of catalytic amount of pyridinium *p*-toluenesulphonate[23] afforded the α-aryl glycoside **14a**. The spectral data and the specific rotation of (*p*-methyl)phenyl-2,3-dideoxy-4,6-O-isopropylidene-α-D-*erythro*-hex-2-enopyranoside obtained by this method and through the Mitsunobu reaction were found to be identical, thereby confirming that the anomeric configuration of **14a** is α.



16

i. Na_2CO_3, MeOH, 3h, room temperature
ii. 2,2-dimethoxypropane, pyridinium *p*--toluenesulfonate (cat.), 1h, room temperature, 30%

Scheme 4

The Mitsunobu reaction of glycal **13** was found to be successful with various nucleophiles such as *p*-methoxyphenol, acetic acid, phthalimide and cyclohexane-1,3-dione (Scheme 3 ; Table 2). In all the cases, the reaction afforded the α-anomer as the major products. The anomeric configuration was assigned by comparing the spectral data with that of **14a**.

It is interesting to note that in the Mitsunobu reaction of glycal **13** with cyclohexane-1,3-dione, an ambident nucleophile, alkylation had occurred through the oxygen and not through the carbon as evidenced from the ^{13}C NMR spectrum of the anomeric mixture **14e** and **15e** isolated after column purification. The anomers, however, were not separated. The ^{13}C NMR spectrum displayed signals at δ 91.936(d) and δ 94.972(d) for the anomeric mixture **14e** and **15e** respectively. This region is typical of an anomeric carbon flanked by two oxygen atoms. Further, the ^{13}C NMR spectrum showed three signals for the three methylene groups of the cyclohexane-1,3-dione moiety. If the alkylation had occurred through carbon, one might expect only two signals for the three methylene groups. Even if the C-alkylated product were to exist in the enolic form, because of rapid isomerisation of one enol to the other, the two methylene groups on either side of the carbonyl carbon become equivalent and hence only two signals should be obtained for the methylene groups. Also, the ^{13}C NMR spectrum displayed a signal at δ 105.415 as a doublet, which is due to the olefinic carbon adjacent to the carbonyl group. Thus, from the ^{13}C NMR spectrum, it is clear that **14e** and **15e** are products of O-alkylation and not C-alkylation.[24]

The reaction of glycal **13** with 0.6 equiv. of Ph_3P and DEAD, in the absence of any added nucleophile led to a facile self coupling product, a disaccharide, *viz.*, 1,5-anhydro-2-deoxy-4,6-O-isopropylidene-3-O-(2',3'-dideoxy-4',6'-O-isopropylidene-α-D-*erythro*-hex-2'-enopyranosyl)-D-*arabino*-hex-1-enitol **14f** as the major product with a minor amount of the β-anomer **15f** in moderate yield. The α-anomer **14f** was separated in pure form and characterised thoroughly.

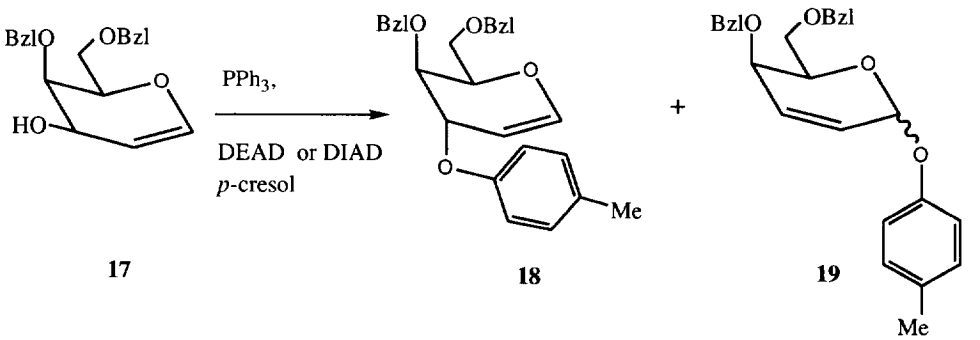
The obtention of anomeric mixture in the Mitsunobu reaction of glycal **13** with various nucleophiles suggests that the anomeric carbon is more electrophilc in such systems and that the reaction probably proceeds through an ionisation mechanism involving the allylic oxonium ion intermediate. Further the Mitsunobu reaction of 4,6-O-isopropylidene-D-*glucal* **13** with different nucleophiles confirms that the reaction is always S_N2' selective irrespective of the nature of the nucleophiles. In all the cases, the reaction occurred at the anomeric centre and products arising out of a direct S_N2 reaction were not at all observed.

The neutral and mild reaction conditions, compatiblity with a variety of nucleophiles, moderate to good yields coupled with the obtention of the α-anomers as the major products render this reaction an efficient alternative to the Ferrier rearrangement. Further, we have demonstrated the generality and the feasibility of this reaction with those nucleophiles which cannot be used under acid catalysed or thermal Ferrier rearrangement.

It is worth mentioning that the stereochemical and regiochemical course of the Mitsunobu reaction of glycals is highly dependant on the stereochemistry of both the allylic hydroxyl group at C-3 and the substituent at C-4. While in the case of *glucal*, the reaction always proceeds at the anomeric centre irrespective of the nature of nucleophiles, in the case of *allal*, the reaction is not very much regiospecific. Guthrie *et al*[20] reported a mixture of products in the reaction of 4,6-O-benzylidene-D-*allal* with benzoic acid.

Fraser-Reid and co-workers[10] obtained only product of a direct S_N2 process *viz.* 4,6-di-O-benzyl-3-O-pentenoyl-D-*gulal* in the Mitsunobu reaction of 4,6-di-O-benzyl-D-*galactal* **17** with n-pentenoic acid. It has been observed by us that the reaction of the same substrate with *p*-cresol as a nucleophile, under similar conditions,

afforded an inseparable mixture of 3-O-aryl derivative **18** and anomeric glycosides **19**in a total yield of 75% among which the *gulal* derivative **18** was the major product (Scheme 5). Attempts to orient the reaction to obtain either the aryl glycosides **19** or the *gulal* derivative **18** as a single product, by changing the reaction condition, temperature, solvent *etc*.. were unsuccessful. Thus it is clear from the above observation the Mitsunobu reaction in this case is also dependant on the nature of the nucleophile.[25]



DIAD = Diisopropyl azodicarboxylate

Scheme 5

Conclusions

In this paper, we have reported a facile synthesis of aryl-2-deoxy-2-methylene glycosides **5**,**6** and **7**,compounds which are not accesible by conventional Ferrier rearrangement, based on the Mitsunobu reaction of 2-deoxy-2-hydroxymethyl glycals **3** and **4**. This method opens up an avenue for a new class of glycosides. The anomeric configurations were unambiguously established by detailed NOE studies, which are otherwise difficult to ascertain by other means. This reaction was also found to be successful with phthalimide as a nucleophile. Also, a neutral, mild and an useful alternative to Ferrier rearrangement for the synthesis of 2,3-dideoxy-hex-2-enopyranosides **14** and **15** has been demonstrated with a variety of nucleophiles. This reaction was found to be general for the synthesis of both alkyl and aryl-2,3-dideoxy-hex-2-eno pyranosides with moderate to high yields. Added advantage is that the reaction has been shown to be successful with such nucleophiles, which cannot be utilised in the acid catalysed or thermal Ferrier rearrangement. Further, the difference in the behaviour of *glucal* and *galactal* towards Mitsunobu conditions was also explained.

Experimental

M.P.s were determined on a Toshniwal melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1310 or on a Shimadzu 470 spectrometer in $CHCl_3$. LRMS and HRMS were

recorded on a Finnigan Mat 8230 mass spectrometer. Optical rotations were measured on a Jasco DIP 370 digital polarimeter. All ^1H NMR spectra were recorded on a Jeol GSX-400 MHz or Bruker 400 MHz spectrometers in $CDCl_3$ using tetramethylsilane as the internal standard. ^{13}C NMR spectra were recorded at 100 MHz on a Jeol GSX-400 or Bruker 400 spectrometers in $CDCl_3$ using tetramethylsilane as the internal standard. Elemental analysis were carried out on a Heraeus CHN-O Rapid analyser. HPLC analysis were done on a Shimadzu LC 5A instrument using reverse phase ODS column and detected in a UV spectrophotometer detector. Preparative separations were done on a Shimadzu LC 8A liquid chromatography. Methanol and water in the ratio 8 : 2 was used as the mobile phase for all HPLC purposes. Thin layer chromatogram were run on microslide glass plates coated with silica gel G (ACME synthetic) with 1mm thickness and viewed in iodine.

Reduction of aldehydes **1** *and* **2** *with benzyltriethylammonium borohydride*:

To a solution of the aldehyde **1** or **2** (4 mmol) in dry CH_2Cl_2 (20 mL) was added benzyltriethylammonium borohydride[17] (4 mmol) in one lot and the reaction mixture was let stand at room temperature for 24h, quenched with aqueous NH_4Cl solution and the organic layer was washed with aqueous $NaHCO_3$ solution, then with water, dried, filtered and concentrated. Purification of the product by column chromatography (hexane : ethyl acetate = 7 : 3) afforded the alcohols **3** and **4** in 85% yield.

1,5-Anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-hydroxymethyl-D-*arabino*-hex-1-enitol 3: Viscous liquid, $[\alpha]_D^{26}$ +40.4 (*c* 0.34, $CHCl_3$); ν_{max}/cm^{-1} 3410 (OH), 1651 (C=C); ^1H NMR (δ *ppm*): 2.30-2.40(1H, br s, OH), 3.66-3.78(3H, m), 3.92(2H, m), 4.06(1H, dd, $J_{6a,6b}$ 12.2 and $J_{6a,5}$ 4.4 Hz, H-6_a), 4.21(1H, m), 4.47-4.70(6H, m, 3xOCH_2Ph), 6.44(1H, s, H-1), 7.16-7.29(15H, m, aromatic); ^{13}C NMR: 61.38(t, CH_2OH), 67.79(t, C-6), 72.46(t, OCH_2Ph), 72.80(t, OCH_2Ph), 73.72(t, OCH_2Ph), 73.65(d, C-4)[26], 74.80(d, C-3)[26], 75.95(d, C-5)[26], 117.76(s, C-2), 126.73(d, aromatic), 127.26(d, aromatic), 127.53(d, aromatic), 127.56(d, aromatic), 127.70(d, aromatic), 127.76(d, aromatic), 127.80(d, aromatic), 127.90(d, aromatic), 128.08(d, aromatic), 128.23(d, aromatic), 128.28(d, aromatic), 128.37(d, aromatic), 137.61(s, aromatic), 137.70(s, aromatic), 137.79(s, aromatic), 143.12(d, C-1).

1,5-Anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-hydroxymethyl-D-*lyxo*-hex-1-enitol 4: Waxy solid, $[\alpha]_D^{27}$ +25.3 (*c* 0.2, $CHCl_3$); ν_{max}/cm^{-1} 3408(OH), 1651(C=C); ^1H NMR (δ *ppm*): 1.99(1H, br s, OH), 3.77(1H, dd, $J_{6a,6b}$ 10.3 and $J_{6a,5}$ 5.4, Hz, H-6_a), 3.86(1H, dd, $J_{6b,6a}$ 10.3 and $J_{6b,5}$ 7.3 Hz, H-6_b)4.07(1H, d, J_{gem} 12.2 Hz, CH_2OH), 4.09(1H, dd, $J_{4,3}$ 3.9 and $J_{4,5}$ 2.9 Hz, H-4), 4.16(1H, d, J_{gem} 12.2 Hz, CH_2OH), 4.29(1H, m, H-5), 4.41(1H, d, $J_{3,4}$ 3.9 Hz, H-3), 4.50(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.59(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.65(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.73(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.88(1H, d, J_{gem} 7.8 Hz, OCH_2Ph), 4.91(1H, d, J_{gem} 7.8, Hz OCH_2Ph), 6.47(1H, s, H-1), 7.31-7.45(15H, m, aromatic); ^{13}C NMR: 62.02(t, CH_2OH), 68.49(t, C-6), 71.57(d, C-3)[26], 73.22(d, C-4)[26], 73.36(t, OCH_2Ph), 73.80(t, OCH_2Ph), 73.86(t, OCH_2Ph), 75.98(d, C-5)[26], 112.52(s, C-2), 128.18(d, aromatic), 128.29(d, aromatic), 128.35(d, aromatic), 128.82(d, aromatic), 128.97(d, aromatic), 138.28(s, aromatic), 138.48(s, aromatic), 138.57(s, aromatic), 143.18(d, C-1); Anal. Found C 74.93, H 6.88 ; $C_{28}H_{30}O_5$ requires C 75.33, H 6.72%.

General procedure for the Mitsunobu reaction of alcohols **3** *and* **4** *with substituted phenols*:

To a solution of alcohol **3** or **4** (2 mmol), Ph3P (2.2 mmol) and substituted phenol (2.2 mmol) in dry benzene (10 mL) was injected DEAD (2.4 mmol) in dry benzene (2 mL) dropwise over a period of 10 min. The reaction was found to be exothermic initially. The reaction mixture was allowed to stir at room temperature for 10h. The precipitated diethyl hydrazinedicarboxylate was filtered and the organic layer was washed with 20% NaOH solution, then with water, dried, filtered and concentrated. The products were purified by column chromatography (hexane ethyl acetate = 9 : 1).

(*p*-methyl)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-α-D-*arabino*-hexopyranoside 5a : Viscous liquid. $[\alpha]_D^{28}$ +54.7 (*c* 1.09, $CHCl_3$); ν_{max}/cm^{-1} 1640(C=C); ^1H NMR (δ *ppm*): 2.27(3H, s, ArCH_3), 3.61(1H, dd, $J_{6a,6b}$ 10.8 and $J_{6a,5}$ 1.9 Hz, H-6_a), 3.71-3.77(2H, m, H-4 and H-6_b), 4.06(1H, td, $J_{5,4} = J_{5,6b}$ 8.3 and $J_{5,6a}$ 1.9 Hz, H-5), 4.41(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.51(1H, d, J_{gem} 10.8 Hz, OCH_2Ph), 4.59(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.63(1H, d, $J_{3,4}$ 8.8 Hz, H-3), 4.75(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.81(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.89(1H, d, J_{gem} 10.8 Hz, OCH_2Ph), 5.22(1H, s, H-7_a), 5.38(1H, s, H-7_b), 5.83(1H, s, H-1), 7.00(2H, d, *J* 7.8 Hz, aromatic), 7.05(2H, d, *J* 7.8 Hz, aromatic), 7.14-7.41(15H, m, aromatic); ^{13}C NMR: 20.55(q, ArCH_3), 68.50(t, C-6), 72.07(d, C-4)[23], 73.32(t, OCH_2Ph), 73.51(t, OCH_2Ph), 74.77(t, OCH_2Ph), 79.69(d, C-3)[23], 81.07(d, C-5)[23], 100.02(d, C-1), 111.25(t, =CH_2), 116.64(d, aromatic), 127.40(d, aromatic), 127.44(d, aromatic), 127.57(d, aromatic), 127.63(d, aromatic), 127.75(d, aromatic), 127.84(d, aromatic), 127.93(d, aromatic), 128.26(d, aromatic), 128.32(d, aromatic), 128.45(d, aromatic), 128.51(d, aromatic), 129.89(d, aromatic), 131.47(s, aromatic), 138.01(s, aromatic), 138.25(s, aromatic), 141.55(s, C-2), 154.19(s, aromatic); Anal. Found C 78.01, H 6.64; $C_{35}H_{36}O_5$ requires C 78.35, H 6.71%.

(*p*-methyl)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-β-D-*arabino*-hexopyranoside 6a : White crystalline solid, m.p. 110 C; $[\alpha]_D^{28}$ -47.2 (*c* 0.2, $CHCl_3$); ν_{max}/cm^{-1} 1640 (C=C); ^1H NMR (δ *ppm*): 2.29(3H, s, ArCH_3), 3.61(1H, dd, $J_{4,3}$ 8.3 and $J_{4,5}$ 7.8 Hz, H-4), 3.67-3.80(3H, m, H-5, H-6_a and H-6_b), 4.14(1H, d, $J_{3,4}$ 8.3 Hz, H-3), 4.49(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.53(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.58(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 4.68(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.80(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.86(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 5.40(1H, s, H-1), 5.45(1H, s, H-7_a), 5.65(1H, s, H-7_b), 6.99(2H, d, *J* 8.3 Hz, aromatic), 7.07(2H, d, *J* 8.3 Hz, aromatic), 7.21-7.40(15H, m, aromatic); ^{13}C NMR: 20.61(q, ArCH_3), 69.72(t, C-6), 73.07(t, OCH_2Ph), 73.44(t, OCH_2Ph), 74.35(t, OCH_2Ph), 75.70(d, C-4)[26], 79.83(d, C-5)[26], 82.12(d, C-3)[26], 97.83(d, C-1), 110.19(t, =CH_2), 116.85(d, aromatic), 127.47(d, aromatic), 127.72(d, aromatic), 127.78(d, aromatic), 127.82(d, aromatic), 127.96(d, aromatic), 128.26(d, aromatic), 128.37(d, aromatic), 128.46(d, aromatic), 129.89(d, aromatic), 131.83(s, aromatic), 138.05(s, aromatic), 138.13(s, aromatic), 138.28(s, aromatic), 140.60(s, C-2), 155.08(s, aromatic); Anal. Found C 78.22, H 6.65; $C_{35}H_{36}O_5$ requires C 78.35, H 6.71%.

1,5-Anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-(*p*-methyl)phenoxymethyl-D-*arabino*-hex-1-enitol 8a : Viscous liquid, $[\alpha]_D^{29}$ +58.6 (*c* 0.17, $CHCl_3$); ν_{max}/cm^{-1} 1664(C=C); ^1H NMR (δ *ppm*): 2.26(3H, s, ArCH_3), 3.70-3.82(3H, m, CH_2OAr and H-5), 3.95(1H, dd, $J_{4,5}$ 8.2 and $J_{4,3}$ 7.1, H-4), 4.18-4.25(2H, m, H-

6_a and H-6_b), 4.31(1H, d, $J_{3,4}$ 7.1 Hz, H-3), 4.51-4.75(6H, m, 3xOCH_2Ph), 6.54(1H, s, H-1), 6.80(2H, d, J 8.5 Hz, aromatic), 7.04(2H, d, J 8.5 Hz, aromatic), 7.16-7.33(15H, m, aromatic-H); ^{13}C NMR: 20.45(q, ArCH_3), 66.04(t, CH_2OAr), 68.12(t, C-6), 73.04(t, OCH_2Ph), 73.25(t, OCH_2Ph), 73.38(d, C-4)[26], 74.21(t, OCH_2Ph), 74.67(d, C-3)[26], 76.76(d, C-5)[26], 109.35(s, C-2), 114.92(d, aromatic), 127.64(d, aromatic), 127.69(d, aromatic), 127.76(d, aromatic), 127.82(d, aromatic), 127.90(d, aromatic), 128.22(d, aromatic), 128.25(d, aromatic), 128.31(d, aromatic), 128.34(d, aromatic), 128.40(d, aromatic), 129.83(d, aromatic), 129.95(d, aromatic), 137.90(s, aromatic), 137.98(s, aromatic), 138.14(s, aromatic), 144.16(d, C-1), 156.48(s, aromatic); Anal. Found C 78.02, H 6.59; $C_{35}H_{36}O_5$ requires C 78.35, H 6.71%.

(*p*-methoxy)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-α-D-*arabino*-hexopyranoside 5b Viscous liquid, $[\alpha]_D^{26}$ +62.9 (*c* 0.42, $CHCl_3$); ν_{max}/cm^{-1} 1638(C=C); ^{1}H NMR (δ *ppm*): 3.63(1H, dd, $J_{6a,6b}$ 10.8 and $J_{6a,5}$ 1.9 Hz, H-6_a), 3.75(3H, s, OCH_3), 3.93(1H, dd, $J_{4,3}$ 7.5 and $J_{4,5}$ 6.8 Hz, H-4), 4.05-4.24(2H, m, H-5 and H-6_b), 4.30(1H, d, $J_{3,4}$ 7.5 Hz, H-3), 4.43(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.52(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 4.60(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.77(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.82(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.90(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 5.23(1H, s, H-7_a), 5.38(1H, s, H-7_b), 5.76(1H, s, H-1), 6.80(2H, d, $J_{8.5}$ Hz, aromatic), 7.04(2H, d, $J_{8.5}$ Hz ,aromatic), 7.14-7.42(15H, m, aromatic); ^{13}C NMR: 55.60(q, ArOCH_3), 68.61(t, C-6), 72.07(d, C-4)[26], 73.35(t, OCH_2Ph), 73.53(t, OCH_2Ph), 74.98(t, OCH_2Ph), 79.75(d, C-3)[26], 81.07(d, C-5)[26], 100.70(d, C-1), 111.25(t, =CH_2), 114.53(d, aromatic), 118.09(d, aromatic), 127.58(d, aromatic), 127.66(d, aromatic), 127.73(d, aromatic), 127.76(d, aromatic), 127.81(d, aromatic), 127.87(d, aromatic), 127.91(d, aromatic), 128.28(d, aromatic), 128.34(d, aromatic), 128.46(d, aromatic), 138.02(s, aromatic), 138.24(s, aromatic), 141.61(s, C-2), 150.33(s, aromatic), 154.89(s, aromatic).

(*p*-methoxy)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-β-D-*arabino*-hexopyranoside 6b Colourless crystal, m.p. 118 C ; $[\alpha]_D^{26}$ -60.8(*c* 0.2, $CHCl_3$); ν_{max}/cm^{-1} 1640(C=C); ^{1}H NMR (δ *ppm*): 3.60(1H, t, $J_{4,5} = J_{4,3}$ 8.3 Hz, H-4), 3.67-3.80(6H, m, H-5, H-6_a, H-6_b and OCH_3), 4.13(1H, d, $J_{3,4}$ 8.3 Hz, H-3), 4.50(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.53(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.58(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 4.68(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 4.80(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 4.86(1H, d, J_{gem} 11.2 Hz, OCH_2Ph), 5.33(1H, s, H-1), 5.45(1H, s, H-7_a), 5.65(1H, s, H-7_b), 6.80(2H, d, J 8.8 Hz, aromatic), 7.06(2H, d, J 8.8 Hz, aromatic), 7.21-7.40(15H, m, aromatic); ^{13}C NMR: 55.63(q, ArOCH_3), 69.69(t, C-6), 73.10(t, OCH_2Ph), 73.42(t, OCH_2Ph), 74.42(t, OCH_2Ph), 75.62(d, C-4)[26], 79.84(d, C-5)[26], 82.19(d, C-3)[26], 98.51(s, C-1), 110.00(t, =CH_2), 114.48(d, aromataic), 118.29(d, aromatic), 127.49(d, aromatic), 127.70(d, aromatic), 127.75(d, aromatic), 127.79(d, aromatic), 127.82(d, aromatic), 127.97(d, aromatic), 128.28(d, aromatic), 128.38(d, aromatic), 128.48(d, aromatic), 138.02(s, aromatic), 138.10(s, aromatic), 138.28(s, aromatic), 140.70(s,C-2), 151.31(s, aromatic), 155.12(s, aromatic); Anal. Found C 75.66, H 6.42; $C_{35}H_{36}O_6$ requires C 76.08, H 6.52%.

1,5-Anhydro-3,4,6-tri-O-benzyl-2-deoxy-2-(*p*-methoxy)phenoxymethyl-D-*arabino*-hex-1-enitol 8b: Viscous liquid, $[\alpha]_D^{27}$ +58.2 (*c* 0.35, $CHCl_3$); ν_{max}/cm^{-1} 1660(C=C); ^{1}H NMR (δ *ppm*): 3.62-3.83(6H, m, H-5, OCH_3 and CH_2OAr), 3.94(1H, dd, $J_{4,5}$ 8.3 and $J_{4,3}$ 7.1 Hz, H-4), 4.20(2H, m, H-6_a and

H-6_b), 4.32(1H, d, $J_{3,4}$ 7.1 Hz, H-3), 4.51-4.78(6H, m, 3xOCH_2Ph), 6.58(1H, s, H-1), 6.81(2H, d, J 7.8 Hz, aromatic), 7.20-7.40(17H, m, aromatic); ^{13}C NMR: 55.67(q, ArOCH_3), 66.76(t, CH_2OAr), 68.15(t, C-6), 73.06(t, OCH_2Ph), 73.28(t, OCH_2Ph), 73.42(d, C-4)[26], 74.20(t, OCH_2Ph), 74.64(d, C-3)[26], 76.81(d, C-5)[26], 109.38(s, C-2), 114.57(d, aromatic), 116.20(d, aromatic), 127.69(d, aromatic), 127.73(d, aromatic), 127.76(d, aromatic), 127.81(d, aromatic), 127.85(d, aromatic), 127.91(d, aromatic), 128.28(d, aromatic), 128.37(d, aromatic), 128.45(d, aromatic), 137.92(s, aromatic), 137.96(s, aromatic), 138.14(s, aromatic), 144.22(d, C-1), 152.69(s, aromatic), 163.92(s, aromatic).

(*p*-methyl)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-α-D-*lyxo*-hexopyranoside 7a : Viscous liquid, $[\alpha]_D^{26}$ +37.2 (*c* 0.1, $CHCl_3$); ν_{max}/cm^{-1} 1638(C=C); ^{1}H NMR (δ *ppm*): 2.32(3H, s, ArCH_3), 3.50-3.70(2H, m, H-6_a and H-6_b), 4.10(1H, m, H-4), 4.31(1H, t, $J_{5,4} = J_{5,6a}$ 6.1 Hz, H-5), 4.37(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.43(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.63(1H, m, H-3), 4.71(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.72(1H, d, J_{gem} 12.2 Hz,OCH_2Ph), 4.81(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.98(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 5.38(1H, s, H-7_a), 5.54(1H, s, H-7_b), 5.90(1H, s, H-1), 7.00(2H, d, J 8.8 Hz, aromatic), 7.10(2H, d, J 8.8 Hz, aromatic), 7.24-7.45(15H, m, aromatic); ^{13}C NMR: 20.55(q, ArCH_3), 69.03(t, C-6), 71.32(d, C-4)[26], 71.69(t, OCH_2Ph), 73.30(t, OCH_2Ph), 74.18(t, OCH_2Ph), 75.29(d, C-3)[26], 78.03(d, C-5)[26], 100.51(d, C-1), 112.23(t, =CH_2), 116.83(d, aromatic), 127.17(d, aromatic), 127.53(d, aromatic), 127.61(d, aromatic), 127.73(d, aromatic), 128.15(d, aromatic), 128.28(d, aromatic), 128.40(d, aromatic), 128.44(d, aromatic), 129.88(d, aromatic), 131.49(s, aromatic), 137.99(s, aromatic), 138.31(s, aromatic), 138.58(s, aromatic), 140.07(s, C-2), 154.52(s, aromatic).

(*p*-methoxy)Phenyl-3,4,6-tri-O-benzyl-2-deoxy-2-methylene-α-D-*lyxo*-hexopyranoside 7b : Viscous liquid, $[\alpha]_D^{28}$+52.2 (*c* $CHCl_3$); ν_{max}/cm^{-1} 1638(C=C); ^{1}H NMR (δ *ppm*): 3.55-3.58(2H, m, H-6_a and H-6_b), 3.75(3H, s, CH_3), 4.05(1H, m, H-4), 4.28(1H, t, $J_{5,6a} = J_{5,4}$ 6.8 Hz, H-5), 4.36-4.94(7H, m, H-3 and 3xOCH_2Ph), 5.33(1H, s, H-7_a), 5.49(1H, s, H-7_b), 5.77(1H, s, H-1), 6.79(2H, d, J 9.3 Hz, aromatic), 7.01(2H, d, J 9.3 Hz, aromatic), 7.19-7.41(15H, m, aromatic); ^{13}C NMR: 55.62(q, ArOCH_3), 69.20(t, C-6), 71.36(d, C-4)[26], 71.71(t, OCH_2Ph), 73.35(t, OCH_2Ph), 74.17(t, OCH_2Ph), 75.30(d, C-3)[26], 78.04(d, C-5)[26], 101.23(d, C-1), 112.23(t, =CH_2), 116.01(d, aromatic), 127.19(d, aromatic), 127.58(d, aromatic), 127.63(d, aromatic), 127.75(d, aromatic), 127.79(d, aromatic), 127.85(d, aromatic), 128.19(d, aromatic), 128.31(d, aromatic), 128.37(d, aromatic), 128.46(d, aromatic), 138.01(s, aromatic), 138.55(s, aromatic), 140.13(s, C-2), 150.65(s, aromatic), 154.90(s, aromatic).

Mitsunobu reaction of alcohol **4** *with phthalimide:*

To a mixture of alcohol **4** (3 mmol), Ph_3P(3.3 mmol) and phthalimide (3 mmol) in dry benzene (10 mL) was injected DEAD (3.6 mmol) in dry benzene (2 mL) over a period of 10 min. The reaction mixture was stirred at room temperature for 15h. The precipitated diethyl hydrazinedicarboxylate was filtered, the solvent was concentrated. Chromatography (hexane ethyl acetate 7 : 3) afforded the product **10.**

1N-(N-phthaloyl)3,4,6-tri-O-benzyl-2-deoxy-2-methylene-α-D-*lyxo*-hexopyranose 10: Viscous liquid, $[\alpha]_D^{27}$ +9.8 (*c* 0.17, $CHCl_3$); ν_{max}/cm^{-1} 1770, 1715 (C=O); 1H NMR (δ *ppm*): 3.57(2H, dd, J 6.3

and 2.4 Hz, H-6_a and H-6_b), 4.08(1H, m, H-4), 4.34(1H, t, $J_{5,6a}$= $J_{5,4}$ 6.3 Hz, H-5), 4.37(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.42(1H, d, J_{gem} 11.7 Hz, OCH_2Ph), 4.65(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.73(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.78(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 4.92(1H, d, J_{gem} 12.2 Hz, OCH_2Ph), 5.10(1H, d, $J_{3,4}$ 1.9 Hz, H-3), 5.30(1H, s, H-7_a), 5.61(1H, s, H-7_b), 6.46(1H, s, H-1), 7.22-7.87(19H, m, aromatic); ^{13}C NMR: 68.96(t, C-6), 72.04(t, OCH_2Ph), 73.41(t, OCH_2Ph), 73.73(t, OCH_2Ph), 75.39(d, C-4)[26], 76.56(d, C-3)[26], 78.11(d, C-5)[26], 79.43(d, C-1), 115.00(t, =CH_2), 123.59(d, aromatic), 127.40(d, aromatic), 127.52(d, aromatic), 127.60(d, aromatic), 127.63(d, aromatic), 127.85(d, aromatic), 128.17(d, aromatic), 128.20(d, aromatic), 128.32(d, aromatic), 128.42(d, aromatic), 131.86(s, aromatic), 134.34(d, aromatic), 137.99(s, aromatic), 138.39(s, aromatic), 138.65(s, aromatic), 139.40(s, C-2), 167.84(s, *C*=O)..

Mitsunobu reaction of glucal **13** *with phenols*:

To a stirred solution of glucal **13** (3 mmol), Ph3P (3.3 mmol) and substituted phenol (3.3 mmol) in dry benzene (10 mL) was injected DEAD (3.6 mmol) dissolved in benzene (2 mL) dropwise over a period of 10 min. The reaction mixture was let stir at room temperature for 5h. The precipitated diethyl hydrazine dicarboxylate was filtered, the organic layer was washed with 20% NaOH solution, then with water, dried, filtered and concentrated. Chromatography (hexane ethyl acetate 9 : 1) afforded the products as a mixture of anomers which were separated by preparative HPLC.

(*p*-methyl)Phenyl-2,3-dideoxy-4,6-O-isopropylidene-α-D-*erythro*-hex-2-enopyranoside 14a : Colourless solid, m.p. 121 C , $[\alpha]_D^{27}$ +133.3 (*c* 0.17, $CHCl_3$); ν_{max}/cm^{-1} 1640 (C=C); ^{1}H NMR (δ *ppm*): 1.40(3H, s, CH_3), 1.50(3H, s, CH_3), 2.28(3H, s, ArCH_3), 3.73-3.90(3H, m, H-5 and H-6_a and H-6_b), 4.25(1H, d, $J_{4,5}$ 7.3 Hz, H-4), 5.60(1H, br s, H-1), 5.83(1H, td, $J_{3,2}$ 10.2 and $J_{3,4}$ = $J_{3,1}$ 2.4 Hz, H-3), 6.12(1H, d, $J_{2,3}$ 10.2 Hz, H-2), 6.93(2H, d, *J* 9.2 Hz, aromatic), 7.08(2H, d, *J* 9.2 Hz, aromatic); ^{13} C NMR: 18.99(q, C(*C*H_3)$_2$), 20.57(q, Ar*C*H_3), 29.16(q, C(*C*H_3)$_2$), 62.93(t, C-6), 65.80(d, C-5)[26], 67.47(d, C-4)[26], 93.59(d, C-1), 99.94(s, *C*(CH$_3$)$_2$), 116.83(d, aromatic), 125.91(d, C-3), 129.91(d, aromatic), 131.65(s, aromatic), 132.44(d, C-2), 155.02(s, aromatic); EIMS: 276(M^+), HRMS Found 276.13149, $C_{16}H_{20}O_4$ requires M^+ 276.13616.

(*p*-methyl)Phenyl-2,3-dideoxy-4,6-O-isopropylidene-α-D*erythro*-hex-2-enopyranoside 15a : Viscous liquid, $[\alpha]_D^{28}$ +52.4 (*c* 0.58, $CHCl_3$); ν_{max}/cm^{-1} 1632 (C=C); ^{1}H NMR (δ *ppm*): 1.44(3H, s, CH_3), 1.47(3H, s, CH_3), 2.29(3H, s, ArCH_3), 3.65(1H, ddd, $J_{5,6a}$ 16.7, $J_{5,4}$ 10.4 and $J_{5,6b}$ 6.4, H-5), 3.84-3.93(2H, m, H-6_a, H-6_b), 4.45(1H, dd, $J_{4,5}$ 10.4 and $J_{4,3}$ 2.4 Hz, H-4), 5.78(1H, td, $J_{3,2}$ 9.7 and $J_{3,4}$ = $J_{3,1}$ 2.4 Hz, H-3), 5.86(1H, br s, H-1), 6.10(1H, d, *J* 9.7 Hz, H-2), 6.96(2H, d, *J* 8.9 Hz, aromatic), 7.08(2H, d, *J* 8.9 Hz, aromatic); ^{13}C NMR: 19.11(q, C(*C*H_3)$_2$), 20.57(q, Ar*C*H_3), 29.19(q, C(*C*H_3)$_2$), 62.69(t, C-6), 67.26(d, C-5)[26], 71.90(d, C-4)[26], 97.07(d, C-1), 100.00(s, *C*(CH$_3$)$_2$), 116.76(d, aromatic), 127.05(d, C-3), 129.89(d, aromatic), 132.00(s, aromatic), 132.76(d, C-2), 154.67(s, aromatic); EIMS: 276(M^+); HRMS Found 276.13423, $C_{16}H_{20}O_4$ requires M^+ 276.13626.

(*p*-methoxy)Phenyl-2,3-dideoxy-4,6-O-isopropylidene-α-D-*erythro*-hex-2-enopyranoside 14b: Colourless solid, m.p. 109 C ; $[\alpha]_D^{28}$ +142.7 (*c* 0.23, $CHCl_3$); ^{1}H NMR (δ *ppm*): 1.44(3H, s, CH_3), 1.52(3H, s, CH_3), 3.77(3H, s, OCH_3), 3.78-3.90(3H, m, H-5, H-6_a and H-6_b), 4.24(1H, d, $J_{4,5}$ 7.3 Hz,

H-4), 5.53(1H, br s, H-1), 5.84(1H, dd, $J_{3,2}$ 10.2 and $J_{3,1}$ 2.4 Hz, H-3), 6.11(1H, d, $J_{2,3}$ 10.2 Hz, H-2), 6.82(2H, d, J 9.3 Hz, aromatic), 6.99(2H, d, J 9.3 Hz, aromatic); ^{13}C NMR: 18.99(q, C(CH_3)$_2$), 29.17(q, C(CH_3)$_2$), 55.65(q, ArOCH_3), 62.95(t, C-6), 65.73(d, C-5)[26], 67.50(d, C-4)[26], 94.38(d, C-1), 99.96(s, C(CH_3)$_2$), 114.56(d, aromatic), 118.41(d, aromatic), 125.96(d, C-3), 132.42(d, C-2), 151.18(s, aromatic), 155.04(s, aromatic); EIMS: 292(M^+); HRMS: Found 292.13149, $C_{16}H_{20}O_5$ requires M^+ 292.13108.

(*p*-methoxy)Phenyl-2,3-dideoxy-4,6-O-isopropylidene-β-D-*erythro*-hex-2-enopyranoside 15b: Solid m.p. 66 C, $[\alpha]_D^{29}$ +66.2 (*c* 0.2, $CHCl_3$); ν_{max}/cm^{-1} 1625 (C=C); ^{1}H NMR (δ *ppm*): 1.43(3H, s, CH_3), 1.47(3H, s, CH_3), 3.78(3H, s, OCH_3), 3.67(1H, ddd, $J_{5,6a}$ 16.0, $J_{5,4}$ 10.4 and $J_{5,6b}$ 6.4 Hz, H-5), 3.82-3.97(2H, m, H-6_a and H-6_b), 4.43(1H, d, $J_{4,5}$ 10.4 Hz, H-4), 5.77(1H, d, $J_{3,2}$ 10.3 Hz, H-3), 5.90(1H, br s, H-1), 6.12(1H, d, $J_{2,3}$ 10.3 Hz, H-2), 6.80(2H, d, J 8.7 Hz, aromatic), 6.94(2H, d, J 8.7, aromatic); EIMS: 292(M^+); Anal. Found C 66.12, H 6.98; $C_{16}H_{20}O_5$ requires C 65.75, H 6.85%.

General procedure for the Mitsunobu reaction of glycal **13** *with various nucleophiles:*
DEAD (3.6 mmol) dissolved in dry benzene (2 mL) was slowly injected into a solution of glycal **13** (3 mmol), Ph_3P (3.3 mmol) and nucleophile (3.3 mmol) in dry benzene (10 mL). After the reaction was over, the precipitated diethyl hydrazinedicarboxylate was filtered, the organic layer was concentrated and products were purified by column chromatography.

1-O-Acetyl-2,3-dideoxy-4,6-O-isopropylidene-D-*erythro*-hex-2-enopyranoses 14c and 15c: The anomers were not separated. The glycosidic mixture **14c** and **15c** had m.p. 88-93 C; $[\alpha]_D^{26}$ +37.3 (*c* 0.35, $CHCl_3$); ν_{max}/cm^{-1} 1750(C=O) ^{1}H NMR[27] (δ *ppm*):1.43(3H, s, CH_3), 1.52(3H, s, CH_3), 2.09(3H, s, $OCOCH_3$), 3.66-3.72(1H, dt, $J_{5,6a} = J_{5,4}$ 10.3 and $J_{5,6b}$ 4.9 Hz, H-5), 3.79(1H, t, $J_{6a,6b} = J_{6a,5}$ 10.3 Hz, H-6_a), 3.93(1H, dd, $J_{6b,6a}$ 10.3 and $J_{6b,5}$ 4.9 Hz, H-6_b), 4.24(1H, dd, $J_{4,5}$ 10.3 and $J_{4,3}$ 2.4 Hz, H-4), 5.68(1H, td, $J_{3,2}$ 10.3 and $J_{3,4} = J_{3,1}$ 2.4 Hz, H-3), 6.12(1H, d, $J_{2,3}$ 10.3 Hz, H-2), 6.25(1H, br s, H-1); ^{13}C NMR[27]: 18.93(q, C(CH_3)$_2$), 21.17(q, $COCH_3$), 29.10(q, C(CH_3)$_2$), 62.73(t, C-6), 66.94(d, C-5)[26], 67.09(d, C-4)[26], 88.38(d, C-1), 100.01(s, C(CH_3)$_2$), 124.57(d, C-3), 132.98(d, C-2), 170.02(s, C=O); EIMS: 228(M^+), 213, 185; HRMS Found 228.09944; $C_{11}H_{16}O_5$ requires M^+ 228.09978.

1-N(N-phthaloyl)-2,3-dideoxy-4,6-O-isopropylidene-D-*erythro*-hex-2-enopyranoses 14d and 15d: The anomeric mixture **14d** and **15d** was obtained as a gum , which were not separated. $[\alpha]_D^{26}$ +40.4 (*c* 0.75, $CHCl_3$); ν_{max}/cm^{-1} 1776, 1721 (C=O); ^{1}H NMR (δ *ppm*): 1.39(s), 1.47(s), 1.50(s), 3.60-3.93(m, H-5, H-6_a and H-6_b), 4.19(dd, $J_{4,5}$ 8.1 and $J_{4,3}$ 1.6 Hz, H-4 of **15d**), 4.50(dd, $J_{4,5}$ 8.1 and $J_{4,3}$ 1.6 Hz, H-4 of **14d**), 5.57(td, $J_{3,2}$ 10.2 and $J_{3,4} = J_{3,1}$ 1.6 Hz, H-3 of **14d**), 5.67(td, $J_{3,2}$ 10.2 and $J_{3,4} = J_{3,1}$ 1.6, H-3 of **15d**), 6.00-6.20(m, H-1 and H-2), 7.64-7.82(m, aromatic); ^{13}C NMR: 18.88(q, C(CH_3)$_2$), 19.02(q, C(CH_3)$_2$), 29.05(q, C(CH_3)$_2$), 29.14(q, C(CH_3)$_2$), 62.44(t, C-6), 62.91(t, C-6), 66.97(d, C-5)[26], 67.35(d, C-5)[26], 67.47(d, C-4)[26], 72.37(d, C-4)[26], 72.49(d, C-1), 75.00(d, C-1), 99.69(s, C(CH_3)$_2$), 99.89(s, C(CH_3)$_2$), 123.60(d, C-3), 123.72(d, C-3), 124.65(s, aromatic), 131.75(d, C-2), 131.96(d, C-2), 134.18(d, aromatic), 134.39(d, aromatic), 166.66(s, C=O), 167.56(s, C=O); EIMS: 315(M^+); HRMS Found 315.11408; $C_{17}H_{17}O5_N$ requires M^+ 315.11068.

1-O(cyclohex-1'-ene-3'-one-1'-yl)-2,3-dideoxy-4,6-O-isopropylidene-D-erythro-hex-2-enopyranoses 14e and 15e: The anomeric mixture **14e** and **15e** had a m.p. 110-118 C $[\alpha]_D^{27}$ +167.2 (*c* 0.17, $CHCl_3$); ν_{max}/cm^{-1} 1690 (C=O), 1621(C=C); ^1H NMR(δ *ppm*): 1.43(s), 1.52(s), 2.00-2.40(m), 2.28-2.45(m), 3.63-3.90(m, H-5, H-6_a and H-6_b), 4.21-4.25(m, H-4), 5.60(s, H-1 of **14e**), 5.62(s, H-1 of **15e**), 5.71-5.75(td, H-3), 6.15(d, H-3); ^{13}C NMR: 18.86(q, C(CH_3)$_2$), 20.90(t, CH_2), 20.96(t, CH_2), 28.49(q,C(CH_3)$_2$), 28.69(t, CH_2), 29.00(q, C(CH_3)$_2$), 36.50(t, CH_2), 36.56(t, CH_2), 62.13(t, C-6), 62.60(t, C-6), 66.53(d, C-5)[26], 66.99(d, C-5)[26], 72.08(d, C-4)[26], 91.94(d, C-1), 94.97(d, C-1), 100.04(s, C(CH$_3$)$_2$), 105.42(d, C=C-C=O), 105.70(d, C=C-C=O), 124.22(d, C-3), 125.10(d, C-3), 133.44(d, C-2), 133.91(d, C-2), 175.06(s, C=C-C=O), 175.48(s, C=C-C=O), 199.86(s, C=O), 200.03(s, C=O); EIMS: 280(M^+); HRMS: Found 280.12978; $C_{15}H_{20}O_5$ requires 280.13108.

Procedure for the Mitsunobu self coupling of glycal **13**:
To a solution of glycal **13** (558 mg, 3 mmol) and .Ph_3P (1.8 mmol) in dry banzene (10 mL) was injected DEAD (1.8 mmol) dissolved in dry benzene (2 mL). After the reaction was over (2d), the diethyl hydrazine dicarboxylate was filtered and the organic layer was concentrated. Chromatography (hexane ethyl acetate 8:2) afforded the glycal **14f** (263 mg, 49.5%) in pure form while the glycal **15f** (5.5%) could not be obtained pure.

1,5-anhydro-2-deoxy-4,6-O-isopropylidene-3-O(2',3'-dideoxy-4',6'-O-isopropylidene-α-D-*erythro*-hex-2'-enopyranosyl)-D-*arabino*-hex-1-enitol 14f: Viscous liquid, $[\alpha]_D^{27}$ +127.3 (*c* 0.1, $CHCl_3$); δ_H 1.40(3H, s, CH_3), 1.43(3H, s, CH_3), 1.51(6H, s, 2CH_3), 3.70-3.99(7H, m, H-5', H-6'$_a$, H-6'$_b$, H-6_a, H-6_b and H-4) , 4.18(1H, dd, $J_{4',5'}$ 8.8 and $J_{4',3'}$ 2.5 Hz, H-4'), 4.42(1H, td, $J_{3,4}$ 7.3 and $J_{3,1} = J_{3,2}$ 1.9 Hz, H-3), 4.69(1H, dd, $J_{2,1}$ 6.4 and $J_{2,3}$ 1.9 Hz, H-2), 5.32(1H, br s, H-1'), 5.70(1H, td, $J_{3',2'}$ 10.3 and $J_{3',4'} = J_{3',1'}$ 2.5 Hz, H-3'), 5.97(1H, d, $J_{2',3'}$ 10.3 Hz, H-2'), 6.30(1H, dd, $J_{1,2}$ 6.3 and $J_{1,3}$ 1.9 Hz, H-1); ^{13}C NMR: 19.24(q, C(CH_3)$_2$), 19.43(q, C(CH_3)$_2$), 29.31(q, C(CH_3)$_2$), 29.44(q, C(CH_3)$_2$), 61.97(t, C-6), 63.37(t, C-6'), 65.13(d), 68.00(d), 69.88(d), 72.89(d), 72.95(d), 95.46(d, C-1'), 99.83(s, C(CH$_3$)$_2$), 100.15(s, C(CH$_3$)$_2$), 103.53(d, C-2), 126.91(d, C-3'), 131.61(d, C-2'), 144.70(d, C-1); EIMS: 33 (M^+-15).

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23. Use of acid catalyst such as *p*-toluenesulphonic acid, resulted only in the cleavage of the glycosidic linkage and did not lead to the formation of the ketal.

24. Ambident nucleophiles have been used in Mitsunobu reactions and have been shown to afford products of both C-alkylation ans O-alkylation. See ref.12.
25. The presence of three products (**18** and **19**) was clearly seen from the high resolution ^{1}H NMR (400 MHz) and ^{13}C NMR of the product obtained after column chromatography which showed apparent homogenity in TLC. The products, however, could not be separated even by preparative HPLC.
26. The assignments are purely tentative and are interchangeable. Assignments were done by comparing the ^{13}C NMR data available for monosaccharides. See ref.28.
27. The NMR values (both ^{1} NMR and ^{13}C NMR) values correspond only to the α-anomer present in the mixture of **14c** and **15c**. All the other data (m.p., rotation, IR and MS) correspond to the anomeric mixture.
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