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Pd $(OAc)_2$ Mediated Oxidative Cyclisation of γ,δ - olefinic alcohols : A New Route to C-vinyl furanosides

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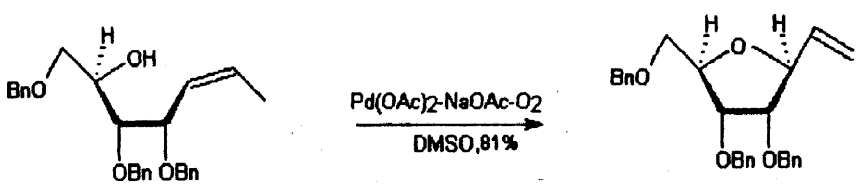
Abstract : An intramolecular oxidative cyclisation protocol, making use of the $Pd(OAc)_2$-$NaOAc$-O_2 system in DMSO, has been developed for the efficient conversion of sugar derived γ,δ -olefinic alcohols into the C-vinyl furanoside class of compounds.

Keywords : γ,δ -olefinic alcohols; intramolecular oxidative cyclisation; C-vinyl furanosides

The increasing interest in bio-active carbohydrates [1,2] stems from a new appreciation that carbohydrates can play an important role in normal and disease processes. Advances made in the understanding of glycobiology, led to the development of the synthetic routes to several glycosyl mimics [3,4,5] such as C-glycosides, C-nucleosides etc. In continuation of our efforts on the synthesis of C-saccharides[6], C-glycosides[7] using Pd(II) reagents, we now describe our results on the synthesis of C-vinyl furanosides[8,9] from γ,δ -olefinic alcohols, by making use of $Pd(OAc)_2$-$NaOAc$-O_2 system in DMSO.



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The intramolecular cyclisation[10] of olefinic alcohols by electrophiles or nucleophiles is one of the best ways to obtain tetrahydrofuran or tetrahydropyran rings. Such a version of cyclisation

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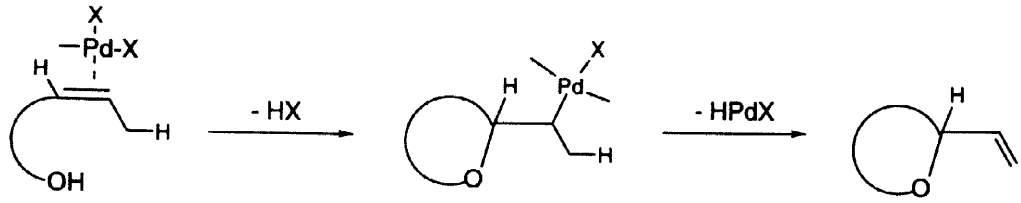
by Pd(II), proceeds through oxypalladation[11,12] adduct (B) as shown in Scheme1, where the use of $PdCl_2$ appears to afford six-membered products, while with $Pd(OAc)_2$, five-membered products are preferred[13]. Under standard reaction conditions using the $Pd(OAc)_2$-NaOAc-O_2 system in DMSO[14,15], the β -hydrogen of the side chain is eliminated predominantly to give 2-vinyl tetrahydrofurans (C)[11,12].

Scheme 1



A **B** **C**

Based on the above information from the literature, a new simple and efficient protocol for the synthesis of C-vinyl furanosides was envisaged from sugar derived olefinic alcohols. Accordingly, the requisite olefinic alcohols **1,3** to **7** were prepared by a Wittig olefination reaction starting with the corresponding lactols. The olefinic alcohols[1] were then subjected to intramolecular oxidative cyclisation, using $Pd(OAc)_2$ (0.1 mmol) and NaOAc (2.0 mmol) in DMSO under a constant stream of O_2 to furnish the C-vinyl furanosides **2,8** to **12** in 75-85% yields, as summarised in Table 1.

The reaction of substrate **1** afforded the pure β -vinyl furanoside **2** (82%),$[\alpha]_D$ + 6.25 (c 0.8,$CHCl_3$), while **7** gave the pure α-glycoside **12** (82%), $[\alpha]_D$+6.35 (c 0.85, $CHCl_3$). Substrates **3, 4** and **5** furnished the β -vinyl furanosides **8,9** and **10** respectively as major products, while **6** gave α - glycoside **11** together with its epimer in ratio 7:1. The diastereomeric mixtures of **9** and **10** were resolved by chromatography into the pure α and β -glycosides **9α** $[\alpha]_D$ -13.33 (c 0.3,$CHCl_3$); **9β** $[\alpha]_D$ - 25.73 (c 1.5, $CHCl_3$); **10β** $[\alpha]_D$ - 20.36 (c 0.9, $CHCl_3$); **10α** $[\alpha]_D$ - 41.99 (c 0.7 $CHCl_3$), while glycosides **8** and **11** could not be resolved into pure isomers. The structures of all the C-vinyl furanosides were arrived at based on the spectral analysis[2].

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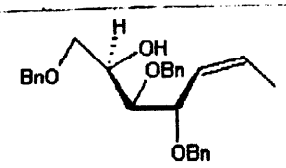
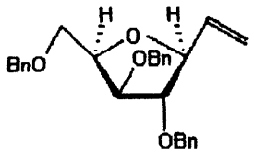
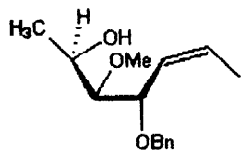
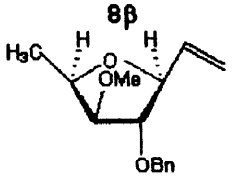
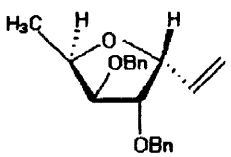
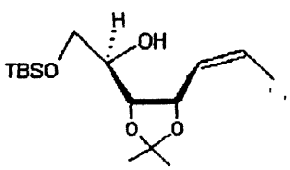
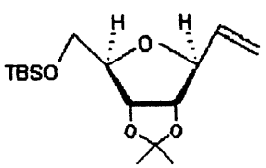
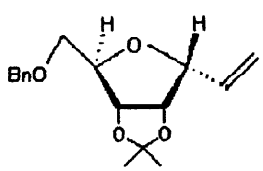
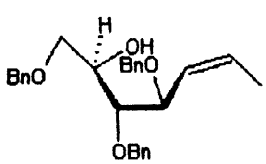
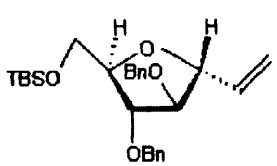
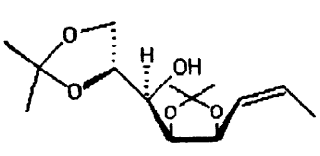
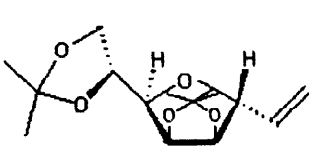
1. All the new compounds gave satisfactory spectral analysis.

2. ^{1}H-NMR data (200 MHz, $CDCl_3$, TMS):**10β**:δ 6.0-5.8 (m, 1H, H-2), 5.33 (br.d, 1H, $J_{1b,2}$ 16.0 Hz, H-1b), 5.15 (br.d, 1H, $J_{1a,2}$ 9.0 Hz, H-1a), 4.62 (dd, 1H, $J_{4,5}$ 6.7, $J_{5,6}$ 3.3 Hz, H-5), 4.35 (dd, 1H, $J_{3,4}$ 5.0 Hz, H-4), 4.25 (dd, 1H, $J_{2,3}$ 6.8 Hz, H-3), 4.05 (App. q, 1H, $J_{5,6}$ 3.6, $J_{6,7}$ 4.5 Hz, H-6), 3.72 (d, 2H, H-7), 1.5, 1.32 (2s, 6H), 0.9 (s, 9H), 0.1 (s ,6H); **10α**:δ 6.05-5.82 (m, 1H, H-2), 5.32 (br.d, 1H, $J_{1a,2}$ 15.0 Hz, H-1a), 5.22 (br.d, 1H, $J_{1b,2}$ 8.15 Hz, H-1b), 4.82 (d, 1H, $J_{4,5}$ 6.12 Hz, H-5), 4.65 (br.t, 1H, H-4), 4.5 (dd, 1H, $J_{3,4}$ 4.0, $J_{2,3}$ 8.0 Hz, H-3), 4.08 (br.t, 1H, H-6), 3.72 (d, 2H, $J_{6,7}$ 4.0 Hz, H-7), 1.58, 1.32 (2s, 6H), 0.92 (s, 9H), 0.1 (s, 6H); **12:** δ 5.62-5.84 (m, 1H, H-2), 5.32 (dd, 1H, $J_{1b,2}$ 15.7 Hz, $J_{1a,1b}$ 2.7 Hz, H-1b), 5.2 (dd, 1H, $J_{1a,2}$ 9.9 Hz, H-1a), 4.75 (dd, 1H, $J_{5,6}$ 4.6 Hz, H-5), 4.62 (d, 1H, $J_{4,5}$ 6.14 Hz, H-4), 4.52 (br.s, 1H, H-3), 4.42-4.3 (m, 1H, H-7), 4.14-3.95 (m, 2H, H-8,8'), 3.74 (dd, 1H, $J_{6,7}$ 9.21 Hz, H-6), 1.5, 1.4, 1.35, 1.3 (4s, 12H).

Table 1: Synthesis of C-vinyl furanosides from γ,δ -olefinic alcohols

Olefin	C-vinyl furanoside	Yield (%)	Ratio
 **3**	 **8β**	83%	3:2
 **4**	 **9β**	79%	3:2
	 **9α**		
 **5**	 **10β**	82%	3:2
	 **10α**		
 **6**	 **11α**	75%	7:1
 **7**	 **12α**	81%	single

Thus, we report a simple and efficient protocol for the conversion of sugar derived olefinic alcohols into C-vinyl furanosides by making use of catalytic quantity of $Pd(OAc)_2$. The vinyl

group in the glycosides may be transformed into several useful compounds, e.g. C-linked amino acids, C-nucleosides etc. This method should find a wide applicability for the synthesis of several glycosyl mimics.

General Procedure : A mixture of olefin (1 mmol), $Pd(OAc)_2$ (0.1 mmol) and NaOAc (2.0 mmol) in DMSO (3 ml) was stirred at 50°C while bubbling a slow stream of O_2 gas for 12-18 hr. The reaction mixture was diluted with water and extracted with ether. Evaporation of solvent and purification of the residue by column chromatography (Si-gel, 9:1 pet.ether-ethyl acetate) furnished the products.

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