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$Pd(II)Cl_2$ Mediated Oxidative Cyclisation of Some 3-Hydroxy 4-Vinyl Furanoside Derivatives to Synthetically Valuable *Bis*-Furanosides

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Abstract: $PdCl_2$ mediated oxidation of 3-hydroxy-4-vinylfuranosides (**Ia-k**) lead to the formation of aldehydes, some of them are '*in situ*' trapped as their lactols (**IIIa,c,e,f,h**)and further converted to bis-furanoside lactones **IVa,c,e,f,h**).

Palladium (II) catalysed oxidation (Wacker process) of terminal olefins to methyl ketones is, probably one of the most well studied organic reactions.[1] Its utility both in industrial processes and in synthetic organic chemistry is too well noted to make a mention in this short communication. Several terminal olefin derivatives possessing various functional groups have been reported to result in the formation of methyl ketones and/or aldehydes[2] under Wacker reaction conditions. However, till date there is no literature precedent to predict the exclusive formation of one of these products for a given substrate. Consequently there is still scope to investigate on a variety of factors to rationalise the formation of aldehyde/ketone with respect to functional groups, substitution pattern and their stereochemical disposition for a given alkene substrate, for utility in organic synthesis.

Our own interest in Palladium(II) catalysed oxidation reactions in the area of synthetic carbohydrate chemistry has earlier resulted in the finding of a new, mild method of deprotection of O-allyl and O-propenyl ethers of several alcohols, in serendipity.[3] Hence, we became interested in optimising reaction conditions required for Wacker oxidation of 3-hydroxy 4-vinylfuranoside derivatives to obtain exclusively aldehydes which *in situ* could be trapped as their lactols and further

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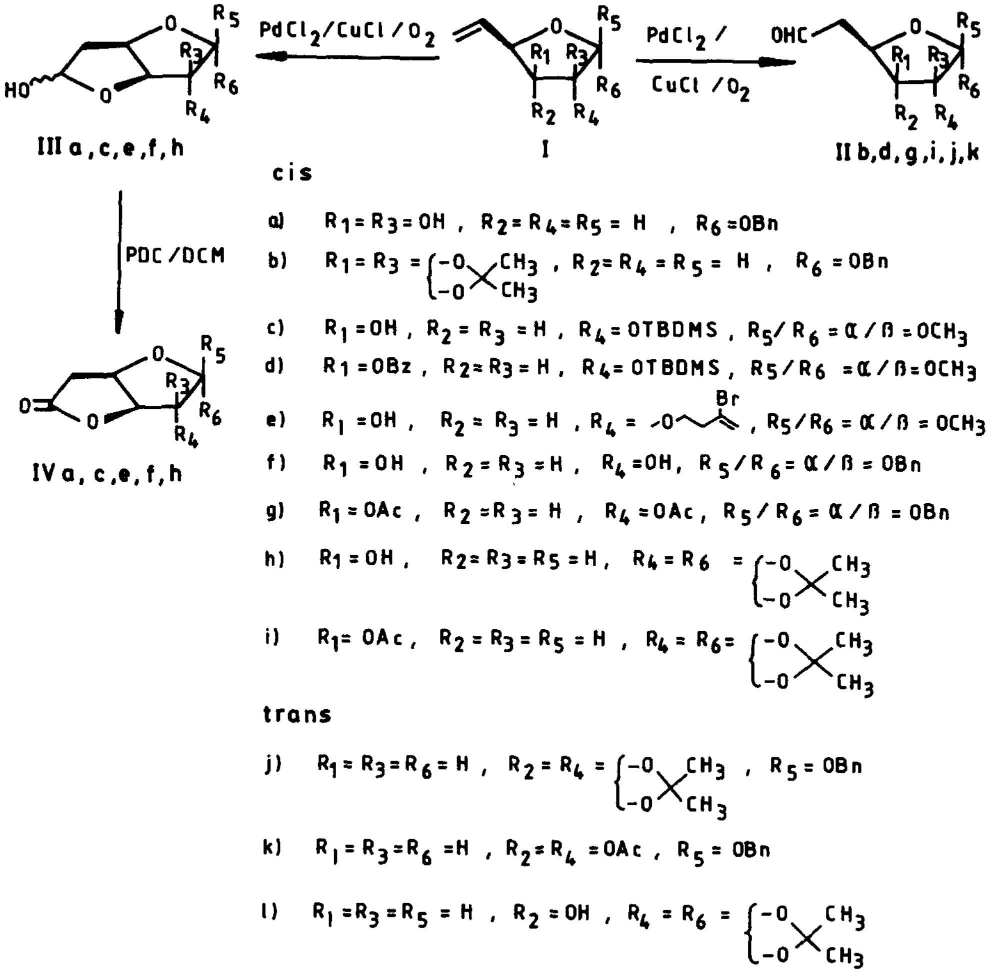
oxidised to *bis*-furanoside lactones, that are valuable synthons. We describe herein our conclusive observations on the Wacker oxidation of 4-vinylfuranoside derivatives (**1a-l**)[4a,b] that led to the synthesis of several valuable chirons (**IV a,c,e,f,h**).

Various furanoside terminal olefins (**Ia-l**) possessing diverse substitution pattern were oxidised under Wacker reaction conditions to obtain aldehydes (**IIb,d,g,i,j,k**) and lactols (**IIIa,c,e,f,h**) respectively (Table 1).



III a,c,e,f,h **I** **II b,d,g,i,j,k**

IV a, c, e, f, h

cis

a) $R_1 = R_3 = OH$, $R_2 = R_4 = R_5 = H$, $R_6 = OBn$

b) $R_1 = R_3 = \left\{ {-O \atop -O} \right. \!\!\times\! {CH_3 \atop CH_3}$, $R_2 = R_4 = R_5 = H$, $R_6 = OBn$

c) $R_1 = OH$, $R_2 = R_3 = H$, $R_4 = OTBDMS$, $R_5/R_6 = \alpha/\beta = OCH_3$

d) $R_1 = OBz$, $R_2 = R_3 = H$, $R_4 = OTBDMS$, $R_5/R_6 = \alpha/\beta = OCH_3$

e) $R_1 = OH$, $R_2 = R_3 = H$, $R_4 = -OCH_2\overset{Br}{C}{=}CH_2$, $R_5/R_6 = \alpha/\beta = OCH_3$

f) $R_1 = OH$, $R_2 = R_3 = H$, $R_4 = OH$, $R_5/R_6 = \alpha/\beta = OBn$

g) $R_1 = OAc$, $R_2 = R_3 = H$, $R_4 = OAc$, $R_5/R_6 = \alpha/\beta = OBn$

h) $R_1 = OH$, $R_2 = R_3 = R_5 = H$, $R_4 = R_6 = \left\{ {-O \atop -O} \right. \!\!\times\! {CH_3 \atop CH_3}$

i) $R_1 = OAc$, $R_2 = R_3 = R_5 = H$, $R_4 = R_6 = \left\{ {-O \atop -O} \right. \!\!\times\! {CH_3 \atop CH_3}$

trans

j) $R_1 = R_3 = R_6 = H$, $R_2 = R_4 = \left\{ {-O \atop -O} \right. \!\!\times\! {CH_3 \atop CH_3}$, $R_5 = OBn$

k) $R_1 = R_3 = R_6 = H$, $R_2 = R_4 = OAc$, $R_5 = OBn$

l) $R_1 = R_3 = R_5 = H$, $R_2 = OH$, $R_4 = R_6 = \left\{ {-O \atop -O} \right. \!\!\times\! {CH_3 \atop CH_3}$

Thus it has been observed that when 3-hydroxy group is in *cis*-relation to the vinyl group in the furanosides (**1a,c,e,f,h**) the products formed were lactols (entry **Ia,c,e,f,h**) due to the trapping of the so formed aldehydes. On the contrary if the 3-hydroxy group is in *trans* orientation (**1***l*) a mixture containing aldehyde and methyl ketone has resulted. It is worthwhile to note that there was no lactol formation in the latter case. It was also observed that when the 3-hydroxy group was protected Wacker oxidation of **1b,d,g,i,j,k** invariably lead to the formation of aldehydes **IIb, d,g,i,j,k** irrespective of the *cis* or *trans* relation of the vinyl and 3-hydroxy group.

Lactol **IIIa**(α/β, 3/1) has been characterised from ^{1}H-NMR spectrum from the appearance of H-1 at ∂ 5.01 and H-6 (α/β) at ∂ 5.52 and ∂ 5.7. ^{13}C-NMR spectrum indicated C-1 at ∂ 100.3, C-6(α) at ∂ 101.3 and C-6(β) at ∂ 109.1. The utility of lactols (**IIIa,c,e,f,h**) was shown by oxidising them further to their *bis*-furanoside synthons (**IVa,c,e,f,h**) (PDC/CH_2Cl_2/4h).

Table 1 : ^{x}PdCl$_2$ mediated oxidation of alkenes

ENTRY	SOLVENT^y	TIME	PRODUCT^5	YIELD^z (in %)
Ia	DMF:H_2O	8 hr	IIIa	81
b	CH_3CN:H_2O	10 hr	IIb	87
c	DMF:H_2O	8 hr	IIIa	81
d	DMF:H_2O	8 hr	IId	82
e	DMF:H_2O	8 hr	IIIe	63
f	CH_3CN:H_2O	12 hr	IIIf	77
g	CH_3CN:H_2O	14 hr	IIg	86
h	DMF:H_2O	6 hr	IIIh	83
i	CH_3CN:H_2O	10 hr	IIi	85
j	CH_3CN:H_2O	13 hr	IIj	76
k	CH_3CN:H_2O	12 hr	IIk	89
l	DMF:H_2O	18 hr	Aldehyde + methyl ketone (1:1)	68

x = PdCl$_2$ (0.2 mole equivalent), CuCl (1 mole equivalent)/O_2

y = 7:1 ratio. For the convenience of isolation of product acetonitrile: water was chosen as solvent of choice in certain reactions.

z = Isolated yields

Thus, in conclusion Wacker oxidation of vinyl furanosides on resulted in the formation of aldehydes. It is perhaps due to the formation of the π-allyl palladium complex of the vinyl furanoside, which being hindered, facilitates the anti-markonikov hydration to give aldehydes as exclusive products. Taking advantage of the above observations various valuable chiral *bis*-furanoside lactols(**IIIa,c,e,f,h**) and *bis*-furanoside lactones (**IVa,c,e,f,h**) have been synthesised.

Typical Experimental Procedure

To a stirred solution of $PdCl_2$ (10 mg, 0.0060 mmole) and CuCl (29 mg, 0.030 mmole) in DMF:H_2O (3 ml, 7:1 ratio) under oxygen atmosphere was added **Ia** (70 mg, 0.030 mmole). The resulting black solution was stirred at room temperature for 8 hr and then extracted with ether. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by SiO_2 (60-120 mesh, 5 gms) column chromatography (EtOAc:hexane 1:1) to afford **IIIa** (60 mg, 81%)

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5. All new compounds gave satisfactory elemental analysis.

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