## A NEW SYNTHETIC METHOD FOR Y-BUTYROLACTOLS BY THE PALLADIUM-CATALYZED REGIOSELECTIVE OXIDATION OF 1-ALKEN-4-OLS

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Summary: 3-Substituted 1-alken-4-ols were oxidized with  $PdCl_2$ -benzoquinone regioselectively at the terminal carbon to afford cyclic hemiacetals ( $\gamma$ -butyrolactols), which were converted to  $\gamma$ -butyrolactones by the Jones oxidation. This reaction was applied to the syntheses of optically active deoxyribose and  $\gamma$ -butenolides.

Oxidation of olefins to carbonyl compounds catalyzed by Pd(II) salts is a useful synthetic method. Particularly it is well-known that terminal olefins can be oxidized selectively to form methyl ketones, which are very useful functional groups for organic synthesis.<sup>1)</sup> Based on this oxidation method, terminal olefins can be regarded as precursors of methyl ketones, or masked ketones. The reaction is useful because terminal olefins are easily available, stable under acidic and basic conditions, and inert to nucleophiles. In addition, many other functional groups, such as carbonyl, hydroxy, halogens, and even internal olefins are not attacked by the Pd(II) catalyst.

The Pd(II)-catalyzed oxidation of terminal olefins is highly regioselective and gives methyl ketones in most cases. But few examples of forming aldehydes from terminal olefins are known. For example, terminal olefins with electron-withdrawing groups are converted to aldehydes or their acetals in alcohol. The Pd(II)-catalyzed oxidation of acrylates or acrylonitrile in alcohol<sup>2</sup>) or ethylene glycol<sup>3</sup> are typical examples. Also formation of aldehydes or their acetals from terminal olefins by the participation of a hydroxy or carbonyl group located at suitable positions has been reported.<sup>4-7</sup> In this paper, we wish to report a regioselective oxidation of 1-alken-4-ols to form cyclic hemiacetals ( $\gamma$ -butyrolactols). In this oxidation, the participation of 4-hydroxy group seems to be important.

Various 1-alken-4-ols were prepared by the reaction of allylic halides with aldehydes promoted by metallic tin and aluminum, and isolated as diastereomeric mixture.<sup>8)</sup> They were subjected to the reaction with  $PdCl_2$  (10 mol%) and p-benzoquinone (3 equiv.) or  $CuCl/O_2$  in wet DMF at a room temperature or 40 °C, and  $\gamma$ -butyrolactols were obtained as major products (Eq. 1). Results of the oxidation of various 3-substituted 1-alken-4-ols are shown in Table 1. The presence of 4-hydroxy group (homoallylic alcohol) is crucial for the high regioselectivity. When the 4-hydroxy group was blocked by acetylation, the oxidation became slower and gave only methyl ketone in a low yield as shown in Eq. 2.<sup>9)</sup>



PdCl<sub>2</sub>-catalyzed Oxidation of 1-Alken-4-ols<sup>a)</sup> Table 1

1-Alken-4-ols <sup>b)</sup>			Reaction Conditions			P	Products		
R <sup>1</sup>	R <sup>2</sup>		Temp/°C	; ;	Time/h	Y	ield/%		
CH <sub>2</sub>	n-CcH12	la	r.t.		3	43	2a	10	
CH <sub>3</sub>	$n-C_{6}H_{13}$	la	40	)	8	<sub>64</sub> f)	2a		
$(CH_2)_7 COOCH_3$	$n-C_5H_{11}$	1ь	60	)	6	74	2ь		
(CH <sub>2</sub> ) <sub>7</sub> COOCH <sub>3</sub>	Н	lc	r.t.		6	58	2c		
QH									
	$\sim$	1d	r.t.		26	62	2d	6	3d
HO	$\sim$	le	40	)	3	61	2e		
EtOOC CO	H // OEt	lf	r.t.		10	61	2£	21	3f
COOCH3	n-C <sub>6</sub> H <sub>13</sub>	lg <sup>c)</sup>	40	)	2	62	2g <sup>d)</sup>		
SO <sub>2</sub> -p-Tol	n-C <sub>6</sub> H <sub>13</sub>	lh	40	)	12	82	2 <b>h</b>		(9)
SO <sub>2</sub> -p-Tol	CH=CHCH <sub>3</sub>	1i 1:C)	r.t.		80	50	$2i^{\alpha}$	10	4 <sup>e)</sup>
OCH2Ph	CH <sub>2</sub> OCOPh	1)°′ 11-C)	r.t.		ð 10	81 97	۲] ۳.		
UCH2Ph	CH20CH2Ph	TK_,	r.t.		τø	87	ZK		

a) Reaction was carried out by using PdCl2 (10 mol%), p-benzoquinone (3 mol equiv.), and wet b) Diastereoisomeric mixtures were used unless otherwise DMF (containing 2% of water). d) Pure  $\beta$ ,  $\gamma$ -trans  $\gamma$ -butyrolactone was noted (except lc and ld). c) Pure erythro isomer. e) As a by-product, 4 was obtained obtained by the Jones oxidation. in 10% yield by the oxidation of the internal olefin without attacking the terminal olefin. f) CuCl-O<sub>2</sub> was used as an oxidant of Pd(0).



Eq. 2

Another important factor in this oxidation is the presence of substituents at 3-position. Thus 3-unsubstituted l-decen-4-ol was converted to the corresponding methyl ketone in 68% yield as shown in Eq. 3. Variuos substituents at 3-position such as alkyl, alkoxy, alkoxycarbonyl, sulfonyl groups were shown to be effective for the hemiacetal formation. Their effect seems to be steric rather than electronic.



This regioselective oxidation has considerable synthetic utility. As one application,  $\gamma$ -butyrolactones 5 were prepared in high yields by the Jones oxidation. They were obtained as mixtures of  $\beta$ ,  $\gamma$ -cis and trans substituted lactones from diastereoisomeric mixture of 1. Also 4-substituted butenolide **6h** was obtained from **2h** by the Jones oxidation, followed by elimination of sulforyl group.



a. CrO<sub>3</sub>-H<sub>2</sub>SO<sub>4</sub>, acetone, 0 <sup>o</sup>C, **5b** 94%, **5g** 100%, **5h** 89%;
b. pyridinium chlorochromate (PCC), CH<sub>2</sub>Cl<sub>2</sub>, r.t., **5i** 61%; c. DBU, CH<sub>2</sub>Cl<sub>2</sub>, 0 <sup>o</sup>C, **6h** 92%.

Preparation of optically active deoxyribose in a protected form was carried out by the oxidation of 3-benzyloxy-4-hydroxy-5-benzoyloxy-1-pentene (lj). The chiral source of this compound lj was derived from optically pure glycelaldehyde. The protected deoxyribose 7 thus obtained was found to be nearly optically pure by comparing its optical rotation with that of an authentic sample derived by the same protection of commercial 2-deoxy-D-ribose.<sup>10</sup>

References

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We prepared the optically active deoxyribose by two methods as shown below.
 Method A:via lj



a. BrMgCH=CH<sub>2</sub>, THF, -20  $^{\circ}$ C, 80%; b. BnCl, 50% aq. NaOH, Et<sub>3</sub>BnNCl (cat.), separation, 40%; c. HCl(1N), MeOH, r.t., 100%; d. BzCN, imidazole, DMF, -10  $^{\circ}$ C, 60%; e. PdCl<sub>2</sub> (see text); f. MeOH, H<sup>+</sup> (HCl).

Method B:via lk



g. 12% (-)-DIPT, 10% Ti(OPr<sup>1</sup>)<sub>4</sub>, 150% Bu<sup>t</sup>OOH, 4A molecular sieves, CH<sub>2</sub>Cl<sub>2</sub>, -20 °C, 90 h, 40%; h. BnCl, 50% aq. NaOH, Et<sub>3</sub>BnNCl (cat.), 70%; i. BnOH, BF<sub>3</sub>-Et<sub>2</sub>O (cat.), CH<sub>2</sub>Cl<sub>2</sub>, -10 °C, 82%.

Optical rotations of the protected-deoxyribose, synthesized by the method A and method B, and the authentic one derived by protection of commercial 2-deoxy-D-ribose (purchased from Aldrich Chemical Co.) are shown below.



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