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Synthesis of α,β-Unsaturated Aldehydes through Palladium Catalyzed Regioselective Hydrogen Migration

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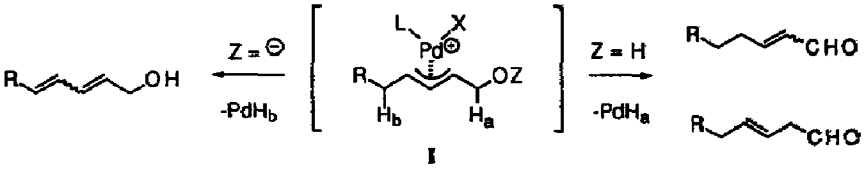
Abstruct: Treatment of cyclic carbonate of 3-alkene-1,2-diols or 4-methylcarbonate of 2-alkene-1,4-diols with a catalytic amount of $Pd(PPh_3)_4$ in aqueous THF or AcOH gave α,β-unsaturated aldehydes in good yields. The reaction can be interpreted by the regioselective 1,4-hydrogen migration of π-allylpalladium intermediate.

It is widely known that the palladium catalyzed elimination reaction of allylic esters and phenyl ethers affords conjugated dienes.[1] This elimination reaction can be explained by the formation of a π-allylpalladium complex, followed by its β-hydrogen elimination. The site-selective β-hydrogen elimination of the π-allylpalladium complex is indispensable to the regioselective formation of the conjugated diene. For example, palladium(0) catalyzed reaction of acyclic 1,3-diene monoepoxides has been shown to afford 1-hydroxy-2,4-dienes.[2] This reaction can be explained by sequential formation of the π-allylpalladium complex **I** and elimination of the β-hydrogen (H_b) located on the opposite site to the hydroxyl group.

On the other hand, elimination of β-hydrogen (H_a) of **I** attached to the site of hydroxyl group will be supposed to give an α,β- and/or β,γ-unsaturated aldehyde.[2-4] We describe herein the synthesis of α,β-unsaturated aldehydes through the regioselective β-hydrogen migration of the π-allylpalladium intermediate **I**, derived from the reaction of cyclic carbonate of 3-alkene-1,2-diols or 4-methylcarbonate of 2-alkene-1,4-diols with palladium catalyst.



Scheme 1

To demonstrate our assumption, the reaction of cyclic carbonate of 3-nonene-1,2-diol **1**, an equivalent of an allylic epoxide,[5] with a catalytic amount of $Pd(PPh_3)_4$ was examined. We found that the reaction in aqueous THF (THF : H_2O = 4 : 1) at 70°C (condition A) gave α,β-unsaturated aldehyde **3** in good yield along with a small amount of β,γ-isomer **4** (entry 1). No stereoselective formation of E or Z isomer could be realized under this condition. When the reaction was carried out in acetic acid at 80°C (condition B), E-isomer of **3** was obtained in a highly selective fashion (entry 2). 4-Methyl carbonate of 2-nonene-1,4-diol **2** was treated with a catalytic amount of $Pd(PPh_3)_4$ in aqueous THF or AcOH to afford almost the same results as those in the case of **1** (entries 4, 5).[6, 7] Whereas carrying out the reaction in THF, the corresopnding 1-hydroxy-2,4-nonadiene (**5**) was obtained as a major product (entries 3, 6). The latter results agreed with those reported previously.[2]

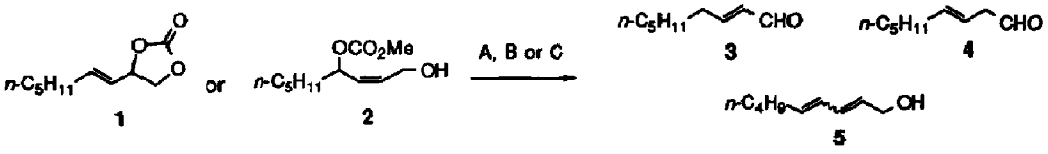
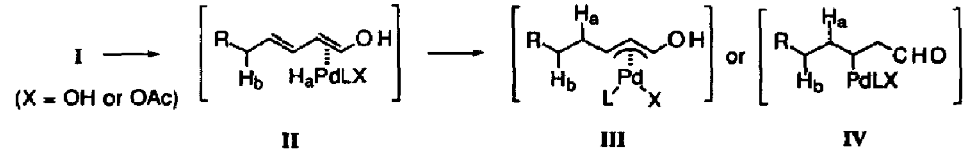


Table 1 : Palladium Catalyzed Reactions of **1** and **2**

entry	reactant	condition [a]	product [b]	E / Z ratio of **3** [b]	Yield(%)
1	**1**	A	**3** and **4** (>99 : 1)	50 : 50	82
2	**1**	B	**3** and **4** (95 : 5)	97 : 3	76
3	**1**	C	**5**	—	72 [c, d]
4	**2**	A	**3** and **4** (95 : 5)	50 : 50	74
5	**2**	B	**3** and **4** (95 : 5)	96 : 4	71
6	**2**	C	**5**	—	75 [c, d]

[a] Reaction conditions A : $Pd(PPh_3)_4$ (2 mol%), THF/H_2O (4 : 1), 70°C / 3 h B : $Pd(PPh_3)_4$ (5 mol%), AcOH, 80°C / 2 h C : $Pd(PPh_3)_4$ (5 mol%), THF, 70°C / 1 h. [b] The ratio was determined by 500 MHz ^{1}H-NMR. [c] 1 : 1 Mixture of stereoisomers. [d] **3** and **4** were isolated in ca 5% yield.

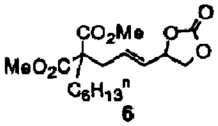
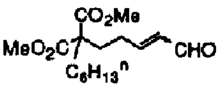
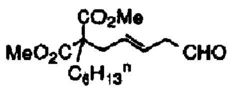
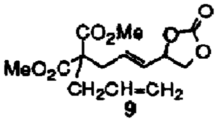
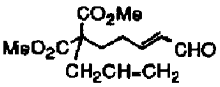
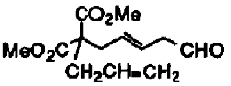
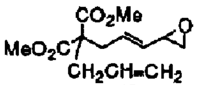
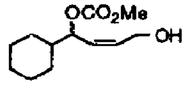
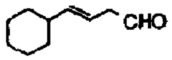
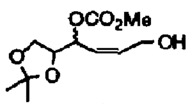
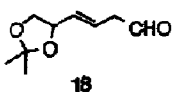
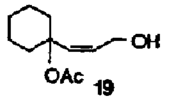
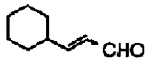
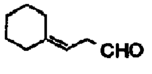
These results indicate that the course of the reaction can be controlled by proper choice of solvent. In a protic solvent such as aqueous THF and AcOH, β-hydrogen (H_a) attached to the site of hydroxyl group was eliminated from π-allylic intermediate I (Z=H) leading to the π-dienepalladium hydride complex **II**. Formation of α,β-unsaturated aldehyde would be interpreted by the re-addition of the hydrogen (H_a) of the complex **II**, followed by elimination of palladium hydride species from the π-complex **III** or the σ-complex **IV** thus obtained.[2] To clarify the reaction mechamism, the reactions of **1** and **2** with $Pd(PPh_3)_4$ in THF / D_2O (4 : 1) or CH_3CO_2D were examined. In each case, no deuterium was incorporated in the product **3**. These results exclude the possibility *via* hydrolysis of dienols from the complex **II** in the reaction media, and indirectly support 1,4-migration of hydrogen.[3d] The detailed mechanistic study is now in progress.



Scheme 2

Several examples for the synthesis of α,β-unsaturated aldehydes are summarized in Table 2.[8] The reaction in AcOH proceeded regioselectively to form α,β-unsaturated aldehydes with high E selectivity. This reaction was not affected by ester or carbon-carbon double bond in the molecule. As expected, 1,3-diene monoepoxide derivative 12 also gave α,β-unsaturated aldehyde 10 predominantly (entry 5). In contrast to the

Table 2. Palladium Catalyzed Regioselective Hydrogen Migration

entry	reactants	condition [a]	products [b]		ratio of αβ : βγ isomers [b]	Yield (%)
1	 6	A	 7 (E : Z = 50 : 50)	 8	85 : 15	75
2	6	B	7 (E : Z = 98 : 2)	8	95 : 5	86
3	 9	A	 10 (E : Z = 44 : 56)	 11	90 : 10	66
4	9	B	10 (E : Z = 95 : 5)	11	97 : 3	86
5	 12	B	10 (E : Z = 98 : 2)	11	98 : 2	60
6	 13	A	 14 (E : Z = 50 : 50)	 15	93 : 7	91
7	13	B	14 (E : Z = 98 : 2)	15	99 : 1	87
8	 16	B	 17 (E : Z = 98 : 2)	 18	>99 : 1	69 [c]
9	 19	A	 20 (E : Z = 80 : 20)	 21	43 : 57	77

[a] Reaction conditions A : Pd(PPh$_3$)$_4$ (2 mol%), THF / H$_2$O (4 : 1), 70°C / 3h B : Pd(PPh$_3$)$_4$ (5 mol%), AcOH, 80°C / 2 h [b] The ratio was determined by 500 MHz ^{1}H-NMR [c] To diminish deacetalization, the reaction was stopped within 30 min.

highly selective formation of α,β-isomers (entries 1-4), tertiary acetate **19** gave a significant amount of β,γ-unsaturated aldehyde derivative presumably due to its relatively high stability (entry 9).

The present reaction provides a useful method for the regio- and stereoselective synthesis of α,β-unsaturated aldehydes, which are fundamental and useful intermediates in organic synthesis, from cyclic carbonate of 3-alkene-1,2-diols or 4-methylcarbonate of 2-alkene-1,4-diols.

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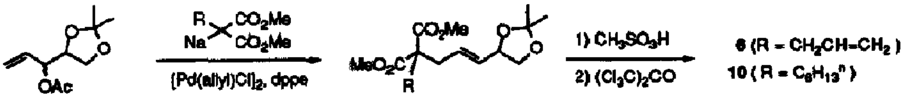
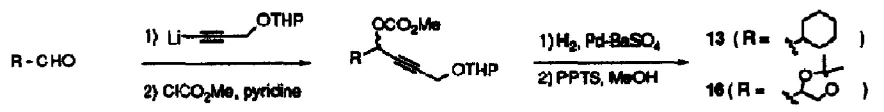
6. Z isomer of **1** and E isomer of **2** gave almost the same results. Therfore, the stereochemistry of starting alcohols did not affect this reaction.
7. The E / Z (1 : 1) mixture of **3** was isomerized to E-isomer in condition A, and even in acetic acid at 80°C Z-isomer was slowly transformed to E-isomer. Accordingly, E-selectivity might be contributory to the isomerization of α,β-unsaturated aldehydes.
8. Substrates were easily prepared as shown in equations i and ii.



(i)



(ii)

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