

Communications

Complete Reverse Regioselection in Wacker Oxidation of Acetonides and Cyclic Carbonates of Allylic Diols

Suk-Ku Kang,* Kyung-Yun Jung, Jea-Uk Chung, Eun-Young Namkoong, and Tae-Hyun Kim

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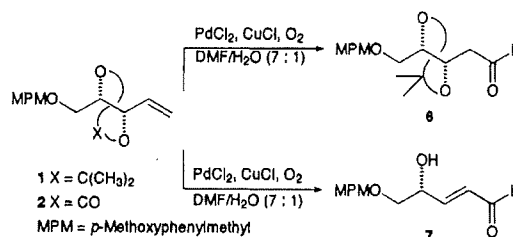
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The palladium(II)-catalyzed oxidation of terminal olefins to methyl ketones (Wacker process) is well established both as an industrial process and an organic synthetic reaction.¹ This reaction appears to involve Markovnikov hydration of the complexed double bond followed by oxidation in a one-step conversion to a methyl ketone.² Thus, terminal olefins can be regarded as masked methyl ketones. Although this process is well-known for the conversion of higher olefins to methyl ketones, few reports have involved preferential aldehyde formation.³ Furthermore, it is reported⁴ that anti-Markovnikov addition occurs in the presence of a heteroatom (i.e., N atom or electron-withdrawing group), whereas terminal olefins bearing neighboring γ -alkoxy or γ -acetoxy functions were oxidized^{1b} to the corresponding methyl ketones.

Because the direct formation of an aldehyde *via* attack at the terminal carbon of a terminal double bond would be valuable synthetic process, we report here the completely regioselective oxygen-oriented Wacker-type reaction of the acetonides and cyclic carbonates of allylic diols, as shown in Scheme 1.

The results are summarized in Table 1.⁵ The terminal allylic diol **1** was treated with a catalytic amount of PdCl_2 and CuCl under an atmospheric pressure of O_2 in DMF and H_2O , at room temperature for 12 h to afford the expected methyl ketone **5** in 90% yield (entry 1). However, treatment of the acetonide of the allylic diol **2**, under the same conditions at 60 °C for 6 h, afforded the terminal aldehyde **6** as the sole product (presumably due to the anti-Markovnikov hydration) in 93% yield with no

Scheme 1

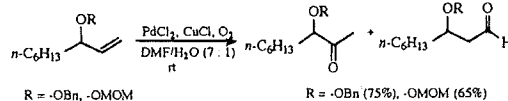


formation of the methyl ketone (entry 2). This result is in contrast to the published result^{1b} that Wacker oxidation of an α -methoxy terminal olefin gives only a methyl ketone. It is presumed that simultaneous chelation of palladium with two adjacent oxygen atoms might induce water to attack in an anti-Markovnikov fashion. As supporting evidence that diol functionality is essential, Wacker oxidation of α - or β -alkoxy olefin did not afford β - or γ -substituted aldehyde as the only product.⁶

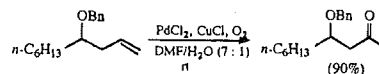
Alternatively, when the diastereoisomer (2*R*,3*S*)-**2** was subjected to the same Wacker conditions, the aldehyde (3*S*,4*R*)-**6** was obtained as the sole product after being stirred at 60 °C for 24 h (entry 3). For the allylic cyclic carbonate **3**,⁷ under the same conditions, γ -hydroxy- α,β -unsaturated aldehyde **7** was obtained in 95% yield (entry 4). By the same methodology, the allylic cyclic carbonate **4** provided the aldehyde **8**,⁸ [$[\alpha]^{25}_{\text{D}} + 48$ (c 0.7, CHCl_3) [lit.^{8b} [$[\alpha]^{25}_{\text{D}} + 46$ (c 0.1, CHCl_3)], which is a cytotoxic lipid peroxidation product,⁹ and also an important chiral synthon for the synthesis of (+)-coriolic acid,^{8a,10} a self-defensive substance for the rice blast disease (entry 5).

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For β -O-(benzyloxy) olefin, only methyl ketone was obtained.



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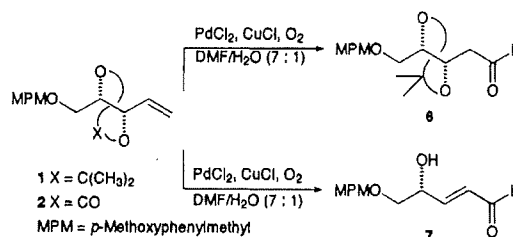
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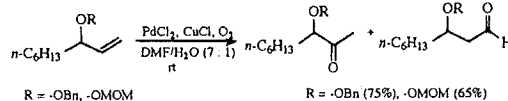


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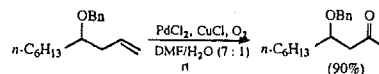
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Table 1. Pd(II)-Catalyzed Oxidation of Terminal Olefins of Allylic Diols, Acetonides, and Cyclic Carbonates^a

Entry	Substrate	Time(h)	Temp(°C)	Products	Yield(%) ^b
1		12	rt		90
2		6	60		93
3		24	60		83
4		12	rt		95
5		12	rt		90

^a All the reactions were run with PdCl₂ (10 mol %), CuCl (1 equiv) in DMF/H₂O (7 : 1) under atmospheric pressure of oxygen.

^b The yields are isolated yields.

internal olefins, it is known^{1b,11} that there is a definite influence by the alkoxy or acetoxy group, which may be explained by coordination of palladium with the oxygen function resulting in control of the regioselection.

The methyl-substituted diol (*E*)-9 was oxidized under Wacker conditions to β -keto diol 12 in 93% yield (entry 1). However, treatment of (*Z*)-9 under the same conditions afforded α -keto diol 13 as the only isolated product in 90% yield (entry 2). It is presumed that in this particular case, steric hindrance around the double bonds considerably affects the regiochemistry of the olefin oxidation. From the (*E*)- or (*Z*)-methyl-substituted acetonides 10, β -keto acetone 14 was obtained (entries 3 and 4). When the cyclic carbonates of (*E*)- or (*Z*)-11 were subjected to Wacker oxidation, γ -hydroxy- α,β -unsaturated ketone 15 was afforded (entries 5 and 6). The results are summarized in Table 2.⁷

A typical procedure is as follows. Preparation of 8: To a stirred solution of PdCl₂ (8 mg, 0.05 mmol) and CuCl

Table 2. Pd(II)-Catalyzed Oxidation of Internal Olefins^a

Entry	Substrate	Time(h)	Temp(°C)	Products	Yield(%) ^b
1		12	rt		93
2		12	rt		90
3		6	60		93
4		6	60		91
5		12	rt		90
6		12	rt		91

^a All the reactions were run with PdCl₂ (10 mol %), CuCl (1 equiv) in DMF/H₂O (7 : 1) under atmospheric pressure of oxygen.

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(42 mg, 0.54 mmol) in DMF and H₂O (7:1, 5 mL) under oxygen atmosphere was added 4 (100 mg, 0.54 mmol). The resulting dark brown solution was stirred at room temperature for 12 h and then extracted with ether. The organic layer was dried over anhydrous MgSO₄ and evaporated *in vacuo*. The crude product was purified by SiO₂ column chromatography (EtOAc:hexanes = 1:2, *R_f* = 0.30) to afford 8 (75.9 mg, 90%).

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Supporting Information Available: Experimental procedures and spectral and analytical data for the new compounds (3 pages).

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