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Palladium(II)-catalyzed Alkoxylation and Acetoxylation of Alkenes

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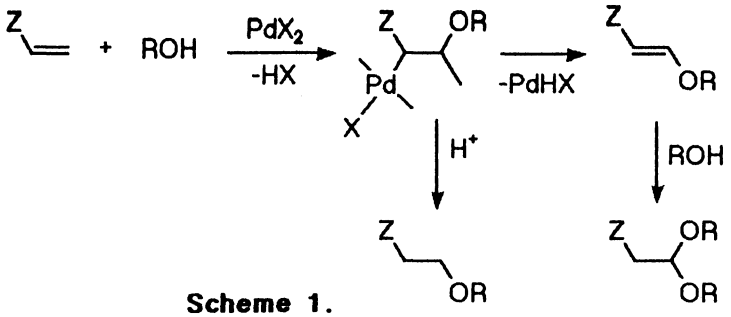
Addition of alcohols or acetic acid to alkenes activated by carbonyl or acetal is catalyzed by $PdCl_2(MeCN)_2$ to give the corresponding ethers and esters.

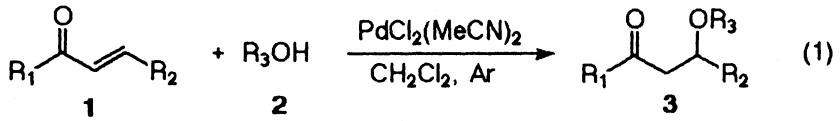
The Pd(II)-promoted addition of oxygen nucleophiles towards alkenes is one of the fundamental pathways in the organic chemistry of palladium.[1-3] The resulting σ-Pd(II) species bearing β-hydrogen atoms generally undergo Pd-H elimination to give aldehydes or ketones in water and vinyl acetates in acetic acid. With alcohols, the resulting vinyl ethers react with additional molecule of alcohols to afford acetals[4] (Scheme 1). Protonolysis of the σ-bonded



Scheme 1.

Pd(II) species would result in the addition of ROH to alkenes; however, there has been no development on the process. We describe here that Pd(II)-catalyzed addition of alcohols and acetic acid to alkenes bearing electron-withdrawing groups (Z) proceeds efficiently.

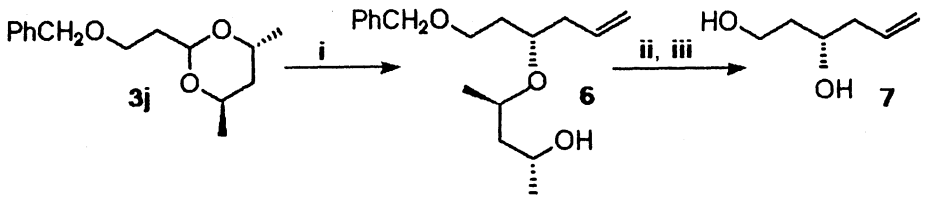
The addition of alcohols to alkenes occurs, when $PdCl_2(MeCN)_2$ is used as a catalyst in CH_2Cl_2 under argon. Protonolysis of the σ-bonded species is accomplished by hydrogen chloride generated in the stage of oxypalladation (Scheme 1). For the alkoxylation, alkenes are required to be activated by electron-withdrawing groups such as carbonyl or acetal. Thus, vinyl ketones 1 react with a variety of alcohols 2 (1 equiv.) to give alkoxylated products 3 in good yields (Eq. 1). Typical results are given in Table 1.



The alkoxylation of terminal alkenes appears to proceed faster than that of internal ones (entries 3 and 8), and steric bulkiness of nucleophiles retards the reaction (entry 4). Acrolein acetal 4 derived from (R,R)-pentane-2,4-diol undergoes the alkoxylation to give 3j in 89% isolated yield (entry 10).[5]

When acetic acid is used as a nucleophile, addition of LiCl is required to promote the acetoxylation. Typically, treatment of phenyl vinyl ketone (1.0 mmol) with $PdCl_2(MeCN)_2$ (10 mol%) in acetic acid (4 mL) in the presence of LiCl (2.1 mmol) at room temperaturer for 20 h under argon gives 5a in 71% yield (entry 11, Table 1). Similarly, esters 5b and 5c can be obtained from the corresponding alkenes (entries 12 and 13). The role of LiCl is considered to prevent the liberation of Cl ligand from the catalyst in acetic acid.

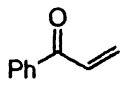
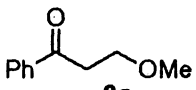
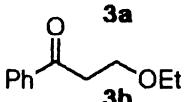
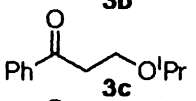
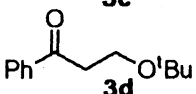
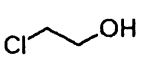
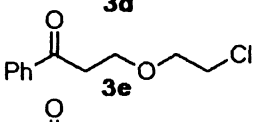
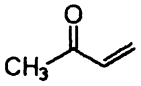
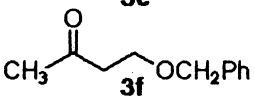
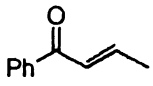
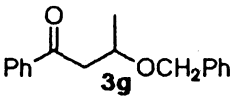
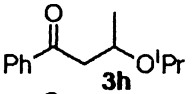
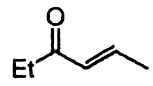
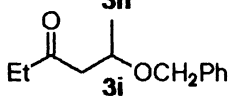
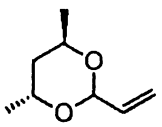
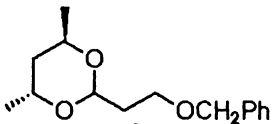
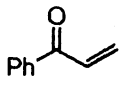
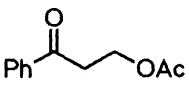
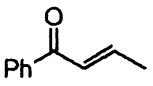
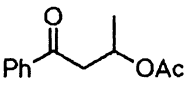
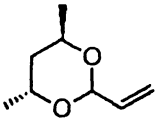
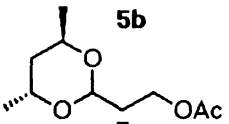
Hydroxylation with water was unable to be observed; however, the corresponding adduct can be readily prepared by benzyloxylation followed by debenzylation. Thus, homochiral acetal 3j becomes useful precursor of



Scheme 2. i, allytrimethylsilane, $TiCl_4$, CH_2Cl_2, -78 °C, 2h; ii, pyridinium chlorochromate, CH_2Cl_2, room temperature, and then K_2CO_3, MeOH; iii, Na, liq. NH_3.

optically active diols as shown in Scheme 2. Diastereoselective cleavage[6] of the acetal 3j with allyltrimethylsilane in the presence of $TiCl_4$ affords 6[7] (78% yield) in 94 %de. Removal of the chiral moiety of 6 followed by debenzylation gives (S)-hexa-5-ene-1,3-diol (7) {70% yield, $[\alpha]_D^{21}$ +9.96 (c 0.70, $CHCl_3$)} in 96 %ee.[8] These results show that the present reaction serves as an entry to optically active diols.

Table 1. Pd(II)-Catalyzed Alkoxylation[a] and Acetylation[b] of Alkenes 1 and 4

Entry	Substrate	ROH	Product	Yield / %
1		MeOH	 **3a**	97
2		EtOH	 **3b**	94
3		^{i}PrOH	 **3c**	98
4		^{t}BuOH	 **3d**	53
5			 **3e**	92
6		$PhCH_2OH$	 **3f**	96
7		$PhCH_2OH$	 **3g**	82
8		^{i}PrOH	 **3h**	48
9		$PhCH_2OH$	 **3i**	89
10	 **4**	$PhCH_2OH$	 **3j**	89
11		AcOH	 **5a**	71
12		AcOH	 **5b**	53
13	 **4**	AcOH	 **5c**	52

a) A mixture of alkene (1 mmol), alcohol (1 mmol), and $PdCl_2(MeCN)_2$ (0.1 mmol) in CH_2Cl_2 (1 mL) was reacted under Ar at room temperature for 20 h. b) Reaction conditions are given in the text. c) Isolated yield. d) Reaction temperature was 50 °C.

References

1) P. M. Maitlis, "The Organic Chemistry of Palladium," Academic Press, New York (1971), Vol. II, pp. 77-126.

2) P. M. Henry, "Palladium Catalyzed Oxidation of Hydrocarbons," Reidel, Dordrecht (1980), pp. 84-147.

3) J. Tsuji, Synthesis, 1984, 369; J. Tsuji, "Organic Synthesis with Palladium Compounds," Springer-Verlag, Berlin (1980), pp. 4-37.

4) T. Hosokawa, T. Ohta, S. Kanayama, and S.-I. Murahashi, J. Org. Chem., 52, 1758, (1987).

5) As a typical procedure, the preparation of 3j is exemplified as follows. In a 50 mL side-armed flask fitted with rubber balloon filled with argon was placed $PdCl_2(MeCN)_2$ (57 mg, 0.22 mmol). Into the flask were added (4R,6R)-4,6-dimethyl-2-vinyl-1,3-dioxane (979 mg, 6.9 mmol) and benzyl alcohol (749 mg, 6.9 mmol) in CH_2Cl_2 (10 mL), and the resulting homogeneous solution was stirred for 20 h at room temperature. The resulting solution was passed through a pad of Florisil (3.0 g, 1.2 cm x 6.0 cm) using ether (50 mL) as eluent. After removal of the solvent under reduced pressure, Kugelrohr distillation gave 3j (1.54 g, 89%): bp 127-130 °C/2 mmHg; R_f 0.58 (SiO_2, hexane:AcEt=7:3); IR (neat) 1153 and 1055 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) 1.18 (d, J=6.0 Hz, 3H, Me), 1.34 (d, J=7.0 Hz, 3H, Me), 1.44-2.13 (m, 4H, $-CH_2-$), 3.58 (t, J=6.5 Hz, 2H, $-OCH_2-$), 3.62-4.42 (m, 2H, -CH-), 4.50 (s, 2H, $-CH_2Ph$), 5.03 (t, J=5.4 Hz, 1H, -CH-), and 7.30 (s, 5H, ArH). Found: C, 71.63; H, 8.88%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.

6) P. A. Bartlett, W. S. Johnson, and J. D. Elliott, J. Am. Chem. Soc., 105, 2088 (1983); A. Mori, J. Fujiwara, K. Maruoka, and H. Yamamoto, Tetrahedron Lett., 24, 4581 (1983); A. Alexakis, P. Mangeney, A. Ghribi, I. Marek, and R. Sedrani, and C. Guir, J. Normant, Pure Appl. Chem., 60, 49 (1988), and references cited therein.

7) 6: bp 134-137 °C/1.5 mmHg; R_f 0.42 (SiO_2, hexane:AcOEt=7:3); IR (neat) 3423(OH), 1100, and 912 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.16 (d, J=6.4 Hz, 3H, Me), 1.20 (d, J=6.4 Hz, 3H, Me), 1.54 (dd, J=4.0 and 6.9 Hz, 1H, $-CH_2-$), 1.58 (dd, J=4.0 and 7.9 Hz, 1H, $-CH_2-$), 1.76 (dt, J=6.2 and 6.2 Hz, 2H, $-CH_2-$), 2.24 (dd, J=6.0 and 6.8 Hz, 2H, $-CH_2-$), 2.71 (brs, 1H, OH), 3.36-4.20 (m, 5H, -OCH-), 4.48 (s, 2H, $-CH_2Ph$), 4.86-5.21 (m, 2H, $H_2C=$), 5.79 (ddt, J=6.8, 9.5, and 18.0 Hz, 1H, =CH-), and 7.30 (s, 5H, ArH). The %de of 6 was determined by GLC using a 25 mm x 0.25 mm chemical bonded glass capillary column (PEG-20M).

8) The (S)-configuration of the newly created chiral center and its %ee were determined by transforming 6 into (S)-hexane-1,3-diol. Thus, removal of the chiral moiety of 6 (pyridinium chlorochromate and then K_2CO_3) followed by hydrogenation (1 atm of H_2, Pd-C) gave (S)-(+)-hexane-1,3-diol {$[\alpha]_D^{24}$ +0.72 (c 1.25, $CHCl_3$)}, and the corresponding (R)-enantiomer {$[\alpha]_D^{25}$ -0.75 (c 0.67, $CHCl_3$)} was obtained by $LiAlH_4$ reduction of optically pure methyl (R)-3-hydroxyhexanoate (A. Tai, T. Kikukawa, Y. Iizuka, T. Sugimura, and T. Harada, Chem. Lett., 1987, 1267.).

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