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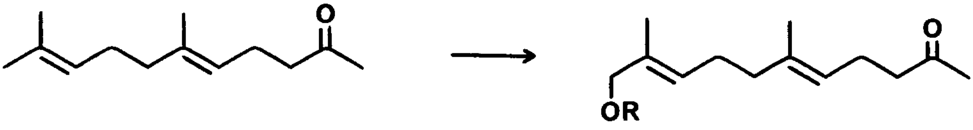
A METHOD FOR THE PALLADIUM-CATALYZED ALLYLIC OXIDATION OF OLEFINS

by
John E. McMurry* and Pavel Kočovský[1]
Department of Chemistry, Baker Laboratory
Cornell University, Ithaca, NY 14853

Abstract: Olefins are converted into allylic acetates by treatment in acetic acid with a catalytic amount of palladium bis(trifluoroacetate) and one equivalent of benzoquinone as oxidant. The reaction is selective for oxidation of a terminal methyl group of geranylacetone.

We were faced recently with a need to prepare keto alcohol **2b** as a starting material for a projected synthesis of germacrane sesquiterpenes. In principle, **2** should result from a simple allylic oxidation on the commercially available geranylacetone (**1**), but in practice this has not been previously achieved. The problem is one of selectivity: Six of the eight saturated carbon centers in geranylacetone are allylic, and the remaining two are alpha to the carbonyl group. After numerous unsuccessful attempts using known methods[2] of allylic oxidation based on the use of SeO_2, we concluded that development of a new method was required.



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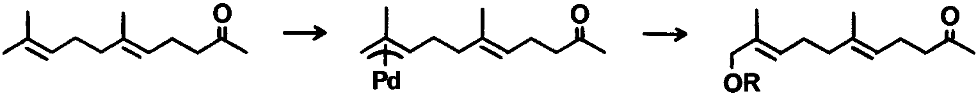
2a (R = Ac)
b (R = H)

Reaction of geranylacetone with a stoichiometric amount of $Pd(OCOCF_3)_2$ is known to take place in a highly selective manner through C-H insertion on a terminal allylic methyl group to give a single π-allylpalladium complex in good yield[3]. Furthermore, π-allyl complexes are known to undergo attack by nucleophiles to yield functionalized allylic products[4]. Thus, the net effect of the two-step Pd insertion/displacement sequence is allylic oxidation. Clearly, however, the synthetic value of the sequence is strongly attenuated by its stoichiometry. We reasoned therefore that the ideal method of selective allylic oxidation would be one in which a catalytic amount of $Pd(OCOCF_3)_2$ would react with geranylacetone in the presence of an oxygen nucleophile and an oxidizing agent. The olefin would first be converted into a terminal π-allyl complex by reaction with Pd^{2+}; the oxygen nucleophile would next displace Pd(0); and the oxidizing agent would oxidize Pd(0) back to its +2 oxidation state to complete the catalytic cycle.



1 2

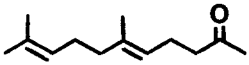
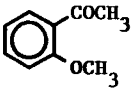
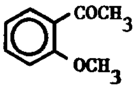
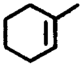
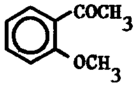
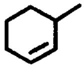
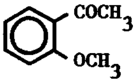
Palladium-induced olefin oxidations have been reported[5], although their study has been from a primarily mechanistic rather than synthetic viewpoint, and no attempts have been made to make them catalytic. After much experimentation with many different oxidants[6], we found that the desired selective allylic oxidation could best be accomplished using a reagent mix containing 0.05 equiv $Pd(OCOCF_3)_2$, 1 equiv benzoquinone[7], and 0.2 equiv *o*-methoxyacetophenone as added ligand[8] in acetic acid solvent[9]. Under these conditions, an 85% isolated yield of allylic acetates **2a** and **2b** was obtained (1.94:1 ratio). Some of our results are summarized in the Table.

As indicated in the Table, product yields and selectivities are influenced both by the oxidant and by the added ligand. With benzoquinone as oxidant and either diethyl malonate or *o*-methoxyacetophenone as an added ligand, product yield was high and an approximately 2:1 preference was observed for formation of terminal acetate **2a**. With duroquinone as oxidant and diethyl malonate as ligand, however, product yield was lower and a 24:1 preference for the allylic rearranged internal acetate **3a** was noted. In no case were products derived from oxidation of other than a terminal methyl group observed.

In a representative procedure, geranylacetone (0.194 g, 1.0 mmol), palladium bis(trifluoroacetate) (0.016 g, 0.05 mmol), *o*-methoxyacetophenone (0.030 g, 0.2 mmol), and benzoquinone (0.108 g, 1.0 mmol) were dissolved in 3 mL acetic acid and stirred for 2 days under an argon atmosphere at room temperature. The dark reaction mixture was then diluted with pentane (3 mL) and filtered through a small pad of silica gel. After washing the silica gel with pentane/ether, the filtrates were combined, washed with water, with 5% aqueous $KHCO_3$, and with brine. Concentration at the rotary evaporator gave a dark residue that was chromatographed on silica gel (9:1 pentane/ether) to give a mixture of allylic acetate products **2a** and **3a** (0.22 g, 85%). Capillary gas chromatography (25 m x 0.2 mm fused-silica Carbowax column) showed the two products to be present in a 1.94:1 ratio. Separation and characterization of the products was accomplished by saponification (K_2CO_3, H_2O, CH_3OH, room temperature overnight) and chromatography of the resultant allylic alcohols **2b** and **3b** on silica gel: alcohol **2b** (0.12 g) NMR ($CDCl_3$) δ 5.31 (t, J = 7 Hz, 1 H), 5.03 (t, J = 7 Hz, 1 H), 3.96 (s, 2 H), 2.11 (s, 3 H), 1.63 (s, 3 H), 1.59 (s, 3 H); alcohol **3b** (0.60 g) NMR ($CDCl_3$) δ 5.09 (t, J = 7 Hz, 1 H), 4.91 (br. s, 1 H), 4.82 (br. s, 1 H), 4.00 (t, J = 7 Hz, 1 H) 2.11 (s, 3H), 1.70 (s, 3 H), 1.61 (s. 3H).

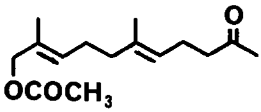
A brief oxidation study of several other olefins was also carried out, as shown in the Table. Good yields were obtained in all cases, although, as expected[10], a mixture of allylically isomeric products was obtained in the oxidation of 1-methylcyclohexene (**6**). 3-Methylcyclohexene (**9**), however, gave only a single product.

TABLE. Palladium-catalyzed Allylic Oxidations

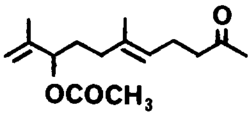
Olefin		Oxidant	Ligand	Temp	Time	Products[a] (ratio)	Yield
		Benzoquinone	-	80°	96 h	2 + 3 (1:1.50)	56%
"		Benzoquinone	$(Ph)_3P$	60°	48 h	2 + 3 (1:1.11)	67%
"		Benzoquinone	$CH_2(COOEt)_2$	35°	24 h	2 + 3 (1.86:1)	73%
"		Benzoquinone		20°	48 h	2 + 3 (1.94:1)	85%
"		Duroquinone	-	90°	96 h	2 + 3 (1:6.14)	51%
"		Duroquinone	$(Ph)_3P$	90°	48 h	2 + 3 (1:22)	31%
"		Duroquinone	$CH_2(COOEt)_2$	90°	48 h	2 + 3 (1:24)	32%
	(4)	Benzoquinone		20°	24 h	5	80%
	(6)	Benzoquinone		60°	1 h	7 + 8 (1.27:1)	80%
	(9)	Benzoquinone		20°	1 h	8	60%

[a] Product purity was established by capillary gas chromatography (25 m x 0.2 mm fused--silica Carbowax column). All products were characterized by IR, MS, and 300 MHz NMR.

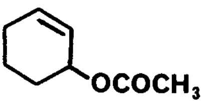
Product structures:



2a



3a



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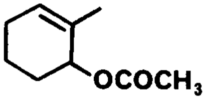

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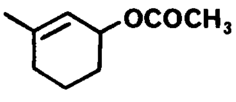

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In light of the above results, we believe that the procedure we have devised represents a useful method of allylic oxidation. Since intermediate π-allylpalladium complexes are presumably present, the selectivity of our method derives from factors different from those normally involved in SeO_2 or radical-type allylic oxidations. Thus, the methods' value is particularly apparent in the oxidation of a diene such as 1, which is known to react selectively with Pd^{2+}.

The utility of this palladium-catalyzed oxidation reaction is moderated by the lack of regiochemical control observed for acetate-ion attack on the the pi-allyl palladium intermediate, which leads to formation of a mixture of allylic acetate products. For many applications, however, such as further palladium-catalyzed alkylations[4], this does not necessarily represent a drawback.

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1. On leave from the Institute of Organic Chemistry, Czechoslovak Academy of Sciences.
2. (a) M. A. Umbreit and K. B. Sharpless, **J. Am. Chem. Soc., 99**, 5526 (1977).
   (b) U. T. Bhalerao and H. Rapoport, **J. Am. Chem. Soc., 93**, 4835 (9171).
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4. For reviews of organopalladium chemistry, see:
   (a) R. Huttel, **Synthesis**, 225 (1970).
   (b) B. M. Trost, **Tetrahedron, 33**, 2615 (1977).
   For a review of palladium-induced oxidation reactions, see: J.-E. Bäckvall, **Accounts Chem. Res., 16**, 335 (1983).
5. (a) W. Kitching, Z. Rappoport, S. Winstein, and W. G. Young, **J. Am. Chem. Soc., 88**, 2054, (1966).
   (b) S. Wolfe and P. G. C. Campbell, **J. Am. Chem. Soc., 93**, 1497, 1499 (1971).
6. Other oxidants tried include $Pb(OAc)_4$, $CuCl_2$, $Hg(NO_3)_2$, $Hg(OAc)_2$, $NaBiO_3$, $NaIO_4$, CrO_3, $(PhCO)_2O_2$, AgOAc, DDQ, and $Ce(NH_4)_6(NO_3)_2$.
7. Use of benzoquinone as oxidant was prompted by some observations of Bäckvall on palladium--catalyzed diene oxidations: J.-E. Bäckvall and R. E. Nordberg, **J. Am. Chem. Soc., 103**, 4959 (1981).
8. In addition to those listed in the Table, other ligands tried include maleic anhydride, succinic acid, maleic acid, phthalic acid, tartaric acid, tributylphosphine, diphos, triethyl phosphite, dimethylaminopyridine, 2,4-pentanedione, o-methoxybenzaldehyde, picolinic acid, and o-methoxybenzyl alcohol.
9. Other solvents tried unsuccessfully include THF, DMF, DMSO, HMPA, ethanol, 2-butanone, acetonitrile, dimethoxyethane, trifluoroacetic acid, formic acid, and isobutyric acid.
10. B. M. Trost and P. E. Strege, **Tetrahedron Lett.**, 2603 (1974).

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