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A NEW PREPARATIVE METHOD FOR 1,3-DICARBONYL COMPOUNDS BY THE REGIOSELECTIVE OXIDATION OF α,β-UNSATURATED CARBONYL COMPOUNDS, CATALYZED BY $PdCl_2$ USING HYDROPEROXIDES AS THE REOXIDANT OF Pd^0

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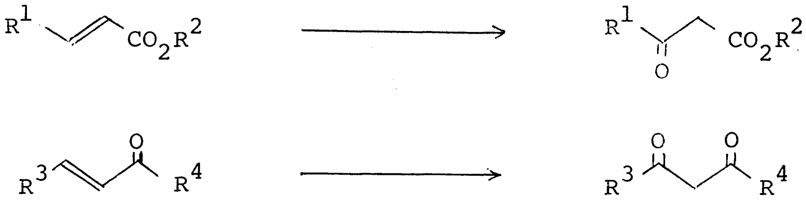
α,β-Unsaturated esters and ketones are oxidized regioselectively to give β-keto esters and 1,3-diketones in good yields in aqueous acetic acid using Na_2PdCl_4 as the catalyst and *t*-butyl hydroperoxide or hydrogen peroxide as the reoxidant of Pd^0.

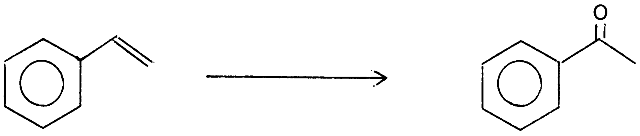
Industrial process of ethylene oxidation to acetaldehyde using aqueous solution of $PdCl_2$-$CuCl_2$ as the catalyst system is well-known as the Wacker process.$^{1)}$ Application of this oxidation method to simple terminal olefins in organic media is a useful synthetic method for methyl ketones,$^{2,3)}$ and we have extensively applied the method to natural product syntheses using $PdCl_2$-$CuCl$-O_2 in aqueous DMF.$^{4)}$ Compared with the facile oxidation of terminal olefins, the oxidation of internal olefins with functional groups is extremely slow under usual conditions. Smidt *et al* reported briefly the oxidation of several α,β-unsaturated carbonyl compounds without experimental details; butyl acrylate and 2-pentenoic acid were oxidized to give acetaldehyde and 2-butanone after subsequent decarboxylation in aqueous medium using stoichiometric amount of $PdCl_2$.$^{5,6)}$ No systematic investigation of the $PdCl_2$-catalyzed oxidation of internal olefins has been reported.

We paid our attention to a possibility that the oxidation of internal olefins with functional groups to functionalized ketones would be a very useful synthetic method for variety of compounds, if the oxidation proceeds with reasonable rate and regioselectivity. From this synthetic viewpoint, we at first have attempted the oxidation of α,β-unsaturated carbonyl compounds, but the reaction under the usual conditions in DMF using $PdCl_2$-$CuCl$-O_2 was very slow. After screening different conditions, we have succeeded to oxidize α,β-unsaturated esters to β-keto esters and α,β-unsaturated ketones to 1,3-diketones regioselectively with satisfactory rate and yields. The results are reported in this paper.



We used Na_2PdCl_4 because of its high solubility. We found that *t*-butyl hydroperoxide and hydrogen peroxide were the best reoxidant of the reduced palladium. Satisfactory solvents were 50% acetic acid, isopropyl alcohol, and *N*-methylpyrrolidone. In methanol or ethanol, the reaction was not clean. THF, DMF, and dioxane were found to be unsatisfactory. The satisfactory rates were observed using 5-20 mol% of Pd^{2+} salt and 1.2-3 equivalents of *t*-butyl hydroperoxide. A mixture of hydrogen peroxide (30%) and acetic acid (1 : 1) is also a good system. The reaction was slow at room temperature, but proceeded smoothly between 50-80°C. Results of the oxidation are shown in the table.

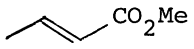
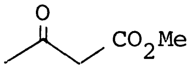
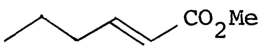
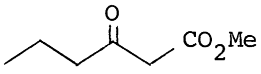
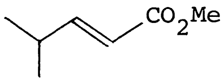
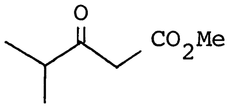
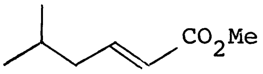
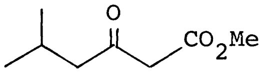
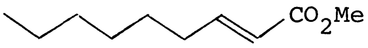
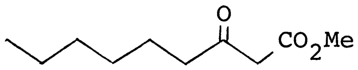
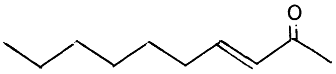
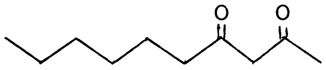
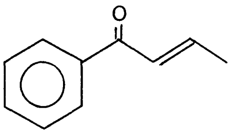
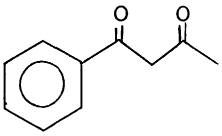
It is worthwhile to consider the role of hydroperoxides in this reaction. As one explanation, the hydroperoxides behave as a strong reoxidant of Pd^0. The ability of hydrogen peroxide to oxidize Pd^0 to Pd^{2+} was reported briefly by Moiseev in the oxidation reaction of ethylene to acetaldehyde.[7)] We tried the oxidation of simple terminal olefins with $PdCl_2/H_2O_2$ system. Styrene was oxidized to acetophenone with Na_2PdCl_4/H_2O_2 system in aqueous *N*-methylpyrrolidone at room temperature in 55% yield. Compared with $PdCl_2/CuCl$ system, the rate of oxidation was very high. 1-Decene and 1-octene were also oxidized smoothly with Na_2PdCl_4/H_2O_2 system, but extensive double bond migration occurred concomitantly to give a mixture of decanones and octanones. Thus this system is not suitable for the oxidation of simple olefins.



1. Na_2PdCl_4 (10 mol%) - H_2O_2 aq.	r. t.	2.5 h	55%
2. $PdCl_2$ (10 mol%) - CuCl (100 mo%)	r. t.	12 h	63%

An alternative mechanism is a stepwise reaction which involves epoxidation of olefins with hydroperoxides and subsequent rearrangement of the epoxides to ketones. But this possibility can be excluded by the following considerations. Epoxidation of olefins with hydroperoxides in an aqueous acidic medium is unknown and unlikely in the presence or absence of palladium catalyst. The palladium-catalyzed rearrangement of epoxy olefins has been reported,[8)] but a zerovalent palladium-phosphine complex is the catalyst, but not Pd^{2+}. To confirm our hypothesis that epoxides are not intermediates, we examined the reaction of styrene oxide under the same conditions of the olefins oxidation. Neither acetophenone nor phenylacetaldehyde was obtained. Rapid hydrolytic ring opening to give glycol was observed. Thus we conclude that hydroperoxides behave as the reoxidant of Pd^0.

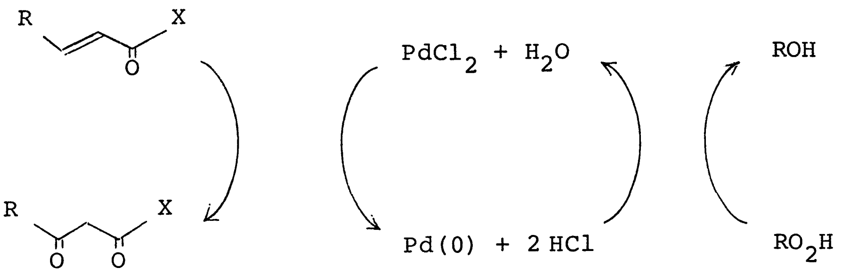
Table

α,β-Unsaturated Carbonyl Compounds^{a}	Product	Yield^{b}	( )^{c}
			(83)
		78	(96)
		64	(96)
		68	(80)
		75	
		59	
		59	

a) Carried out in 50% aqueous acetic acid for 3 h at 50°C using Na_2PdCl_4 (0.2 equiv) and *t*-butyl hydroperoxide (1.2-2.0 equiv).

b) Isolated yields.

c) Determined by G.L.C. using internal standards.



This reaction offers a new and useful synthetic method for various 4-substituted β-keto esters and 1,3-diketones from easily available α,β-unsaturated carbonyl compounds.

General procedure

To a solution of Na_2PdCl_4 (0.2 mmol, 58 mg), *t*-BuOOH (70% in *t*-BuOH, 1.5 mmol, 193 mg) in aqueous acetic acid (50 vol%, 1 ml) was added α,β-unsaturated ester or ketone (1 mmol) in the aqueous acetic acid at room temperature. The solution was heated at 50°C with stirring for 1-5h. After the reaction was complete, the mixture was poured into cold water and extracted with dichloromethane. The combined extracts were washed with 3N-HCl and brine and dried over magnesium sulfate. After removal of the solvent, the residue was purified by column chromatography using ether-hexane to give the corresponding ketone.

References

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