Palladium(II)-catalyzed Selective Oxidation of α,β-Unsaturated Aldehydes to α,β-Unsaturated Carboxylic Acids with Hydrogen Peroxide

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Palladium(II)-catalyzed chemoselective oxidation of α,β-unsaturated aldehydes with hydrogen peroxide to give α,β-unsaturated carboxylic acids was performed. Cinnamaldehyde was effectively catalyzed by palladium(II) trifluoroacetate to generate cinnamic acid in 92% yield under organic solvent-free conditions. The reaction appears to be applicable to various α,β-unsaturated aldehydes.

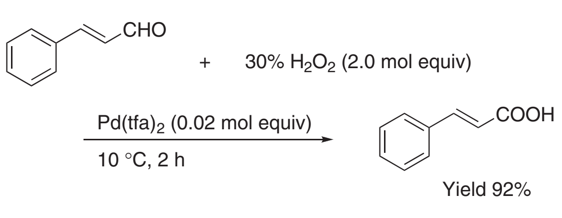
α,β-Unsaturated carboxylic acids are important compounds, known to be some of the most valuable intermediates and precursors for chemical production and pharmaceuticals.[1] Despite the oxidation of aldehydes into carboxylic acids being generally considered to be a simple and downhill reaction,[2] several methods that have been developed for the preparation of α,β-unsaturated carboxylic acids from their aldehyde derivatives require severe and complex reaction conditions.[3] In addition, they use more than equimolar amounts of oxidants, leading to the formation of an equimolar co-product as waste.[3] As a part of the green concept, such toxic oxidants are being replaced by alternative less-toxic reagents.[4] Hydrogen peroxide (H_2O_2) is an ideal oxidant because water is the only side product and the atom efficiency is excellent.[5,6] To our knowledge, however, few synthetic approaches using H_2O_2 have been reported that are catalyzed by Mo and/or W complexes,[7] phase-transfer catalysts,[8] SeO_2,[9] or benzeneseleninic acid[10] for the oxidation of aldehydes,[11] and there is no example dealing with α,β-unsaturated aldehydes as substrates with good chemo-selectivity.[12–14] There is no such example because these compounds undergo many side-reactions (e.g. epoxidation of aldehydes,[10,15] of acids[16] and the Michael addition[15,17]) due to their reactive conjugated double bond. They can also give alcohols and formic acid via the Baeyer–Villiger type fragmentation through hydrolysis.[18] We herein report a practical and simple process for the selective oxidation of α,β-unsaturated aldehydes to their carboxylic acids using H_2O_2 (30% in water) as a terminal oxidant that is effectively catalyzed by $Pd(tfa)_2$ (tfa = trifluoroacetate) under organic solvent-free conditions.

A mixture of (*E*)-cinnamaldehyde (265 mg, 2.0 mmol) and $Pd(tfa)_2$ (13.2 mg, 0.040 mmol) placed in a test tube was stirred at 1500 rpm with a magnetic stirrer at 10 °C, followed by the addition of 30% H_2O_2 (453 mg, 4.0 mmol). After vigorous stirring for 2 h, (*E*)-cinnamic acid was produced in 92% yield (96% selectivity, GC analysis) (eq 1 and Table 1, Entry 2). The reaction proceeded highly chemoselectively to give (*E*)-cinnamic acid, and benzaldehyde (2% yield) and benzoic acid (1% yield) were the only side products, in spite of the organic solvent-free conditions.[15] Table 1 shows the activities of various catalysts. $Pd(OAc)_2$ showed better catalytic activity (70% yield, Entry 4) than those of copper(II) and nickel(II) acetate complexes (0% yields). Among the Pd^{II} complexes, $Pd(tfa)_2$ exhibited excellent activity for the oxidation of (*E*)-cinnamaldehyde (Entry 2). The addition of 1-octene retarded this oxidation of (*E*)-cinnamaldehyde (12% yield) due to the strong coordination of olefin moiety of 1-octene to $Pd(tfa)_2$. $PdCl_2$ was not effective for the catalytic synthesis of cinnamic acid because of lower solubility toward the organic (substrate) phase (6% yield, Entry 7).[19] The addition of NaCl to the H_2O_2–$Pd(tfa)_2$ catalytic system apparently retarded the oxidation, probably due to the generation of $PdCl_2$ in situ (Entry 5). In contrast, Pd^0 complex, $Pd(PPh_3)_4$, was found less effective for the oxidation of (*E*)-cinnamaldehyde (13% yield, Entry 6). The amount of H_2O_2 is also important for the catalysis, and we found that using 2 molar equivalents of H_2O_2 results in optimal performance (Entries 1–3). It is noteworthy that no reaction takes place without the catalyst in spite of the presence of the oxidant with an aldehyde, showing that cationic palladium does accelerate the reaction with excellent chemoselectivity.

Table 1. Various catalysts tested for the oxidation of cinnamaldehyde with hydrogen peroxide[a]

Entry	Catalyst	Yield/%[b]	Selectivity/%[c]
1[d]	$Pd(tfa)_2$	73	97
2		92	96
3[e]		92	95
4	$Pd(OAc)_2$	70	86
5	$Pd(tfa)_2$, NaCl[f]	65	86
6	$Pd(PPh_3)_4$	13	43
7	$PdCl_2$	6	67
8	None	0	0

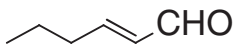
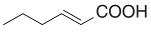
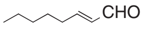
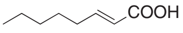
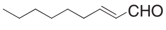
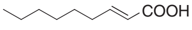
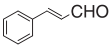
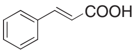
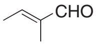
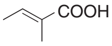
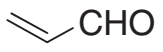
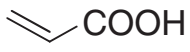
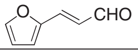
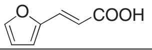
[a]Reaction conditions: (*E*)-cinnamaldehyde (2.0 mmol), 30% H_2O_2 (4.0 mmol), catalyst (0.040 mmol), 10 °C, 1500 rpm, 2 h, unless otherwise stated. [b]Yield and conversion on the basis of (*E*)-cinnamaldehyde, determined by GC analysis with biphenyl as internal standard. [c]Yield/conversion (%). [d]30% H_2O_2 (2.0 mmol) was used. [e]30% H_2O_2 (6.0 mmol) was used. [f]NaCl (0.080 mmol) was added.



(1)

This oxidation system was well applicable to the various α,β-unsaturated aldehydes to give the corresponding carboxylic acids (Table 2).[20] Aliphatic α,β-unsaturated aldehydes were oxidized to the corresponding carboxylic acids in good yields (71, 80, and 73% yields for C6, C8, and C9 α,β-unsaturated aldehydes, respectively, Entries 1, 2, and 4). The reaction with (*E*)-2-methyl-2-butenal proceeded to generate tiglic acid (47% yield, Entry 6). Acrolein was effectively oxidized to generate acrylic acid in 64% yield (Entry 7). Solid α,β-unsaturated alde-

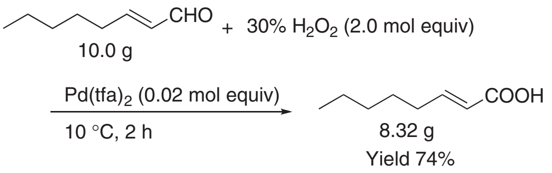
Table 2. Oxidation of various α,β-unsaturated aldehydes with hydrogen peroxide using $Pd(tfa)_2$[a]

Entry	Aldehydes	Products	Yield/%[b]
1			71
2			80
3[c]			74[d]
4			73
5			92
6			47[e]
7[f]			64
8[g]			53

[a] Reaction conditions: (E)-α,β-unsaturated aldehydes (2.0 mmol), 30% H_2O_2 (4.0 mmol), $Pd(tfa)_2$ (0.040 mmol), 10 °C, 1500 rpm, 2 h, unless otherwise stated. [b] Yield and conversion on the basis of (E)-α,β-unsaturated aldehydes, determined by GC analysis with biphenyl as internal standard. [c] The reaction was run using 10 g of (E)-2-octenal. [d] Isolated yield after distillation. [e] Angelic acid (Z isomer) was not observed. [f] 0.5 h. [g] Dimethylacetoamide (0.5 mL) and $Pd(tfa)_2$ (0.060 mmol) were used.

hyde, 3-(2-furyl)acrolein, also gave the corresponding α,β-unsaturated carboxylic acid in 53% yield (Entry 8).

The present method can be carried out on a 10-g scale synthesis of (E)-2-octenoic acid. That is, with 10.0 g of (E)-2-octenal as a starting material, 8.32 g of the corresponding (E)-2-octenoic acid was obtained after distillation of the crude product (74% yield, eq 2 and Table 2, Entry 3).



(2)

In summary, we found a versatile and effective chemoselective Pd-catalyzed oxidation of α,β-unsaturated aldehydes to the corresponding α,β-unsaturated carboxylic acids using H_2O_2 as an oxidant, with the reaction proceeding under mild and environmentally friendly organic solvent-free conditions.

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