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THE DIRECT SYNTHESIS OF α,β-UNSATURATED CARBONYL COMPOUNDS BY Pd(II) PROMOTED DEHYDROGENATION OF ALDEHYDES AND KETONES

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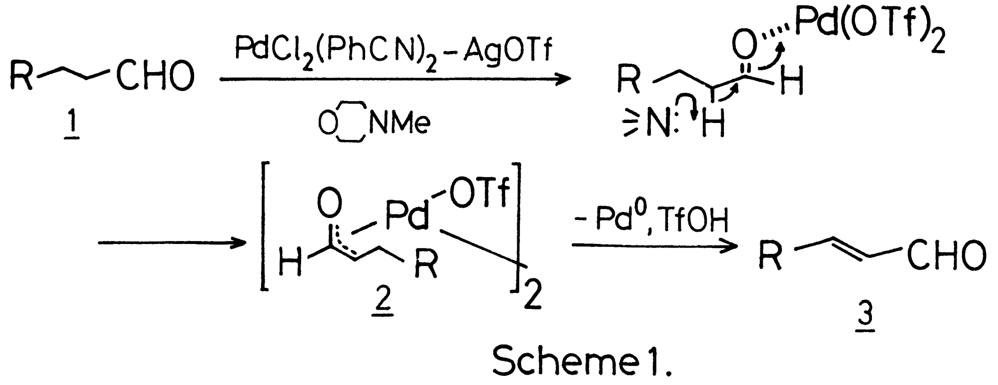
α,β-Unsaturated aldehydes are prepared by the direct dehydrogenation of the corresponding saturated aldehydes by the coupled use of $PdCl_2(PhCN)_2$-$AgOSO_2CF_3$ in the presence of N-methylmorpholine in good yields. α,β-Unsaturated ketones are also prepared via the Sn(II) enolate by a one-pot procedure from the corresponding saturated ketones.

α,β-Unsaturated carbonyl compounds are versatile intermediates in organic synthesis and several methods are known for the synthesis of these compounds starting from the corresponding saturated aldehydes or ketones, for example, α-selenation followed by selenoxide elimination[1)] and palladium (II) catalyzed dehydrosilylation of silyl enol ethers.[2)]

Here we wish to describe convenient methods for the direct synthesis of α,β-unsaturated aldehydes and ketones by Pd(II) promoted dehydrogenation of the corresponding saturated carbonyl compounds.

First, we studied the direct dehydrogenation reaction of saturated aldehydes to the corresponding α,β-unsaturated aldehydes by a coupled use of $PdCl_2(PhCN)_2$-$AgOSO_2CF_3$(AgOTf),[3)] and it was found that 3-phenylpropanal reacted with $PdCl_2(PhCN)_2$-AgOTf in the presence of triethylamine to give cinnamaldehyde in 17% yield. It was assumed that 3-phenylpropanal was converted to oxo-π-allylpalladium[4)] (2) by palladium triflate, generated in situ from $PdCl_2(PhCN)_2$ and AgOTf,[5)] and then so formed oxo-π-allylpalladium was led to cinnamaldehyde by β-elimination as shown in Scheme 1. Various amines were screened and N-methylmorpholine gave the best result. Furthermore, the addition of AgOTf to a mixture of aldehyde, $PdCl_2(PhCN)_2$, and N-methylmorpholine over 45 min gave a better yield in comparison with the addition of AgOTf at one time.



Scheme 1.

A procedure for the preparation of cinnamaldehyde is as follows: Under argon, to a mixture of 3-phenylpropanal (0.4 mmol), $PdCl_2(PhCN)_2$ (0.8 mmol), and N-methylmorpholine (1.6 mmol) in methylene chloride (6 ml) was added a solution of AgOTf (1.6 mmol) in THF (2 ml) over 45 min at room temperature. Stirring was continued for about 12 h, and then aqueous solution of $NaHCO_3$ was added to the resulting mixture. After the insoluble materials were filtered off, the organic materials were extracted with methylene chloride, and the extracts were dried over Na_2SO_4. The solvent was removed, and the residue was purified by preparative TLC to give cinnamaldehyde (0.35 mmol, 88%).

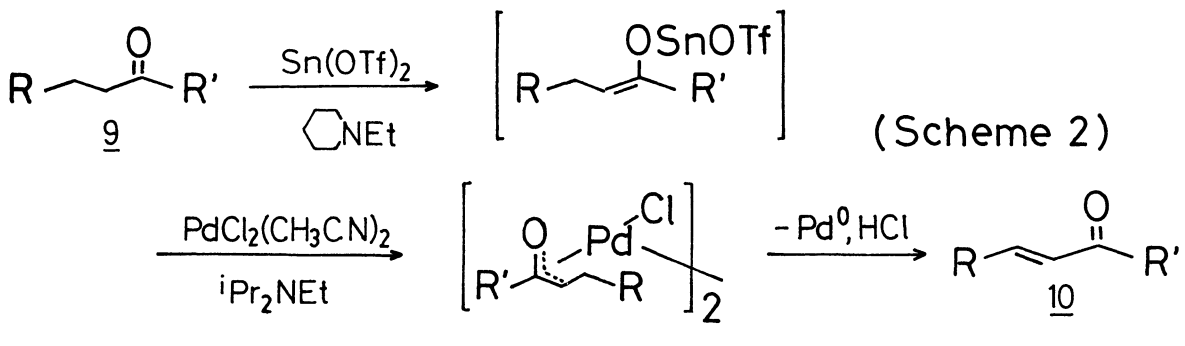
Various α,β-unsaturated aldehydes were prepared by the same method (see Table 1). As shown in Entry 4 and Entry 5 in Table 1, ketone and ester moieties were not affected under these conditions.

Table 1. Preparation of α β-Unsaturated aldehydes.

Entry	Aldehyde		Yield of 3(%)[b)]	Recovery of 1(%)
1	$PhCH_2CH_2CHO$	4	88	–
2	$CH_3(CH_2)_{10}CHO$	5	44 (59)[c)]	25
3	$CH_3CHCl(CH_2)_8CHO$[a)]	6	38 (48)	21
4	$EtCO_2(CH_2)_9CHO$[a)]	7	62 (94)	34
5	$CH_3CO(CH_2)_8CHO$[a)]	8	62 (74)	17

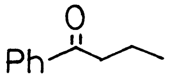
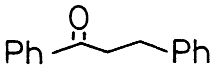
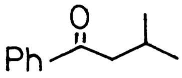
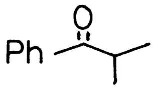
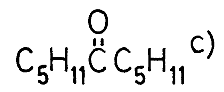
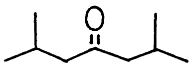
a) This aldehyde was prepared according to the method described in Ref. 6.
b) Isolated yields. All products gave satisfactory NMR and IR spectra.
c) Yields in parenthese were based on consumed starting aldehydes.

Next, the present method was applied to the preparation of α,β-unsaturated ketones by the direct dehydrogenation of saturated ketones. However, the desired oxidation could not be observed probably due to the difficulty of generating the expected oxo-π-allylpalladium from ketone and palladium triflate under the conditions mentioned above. Then, formation of oxo-π-allylpalladium was tried by the replacement of metal enolates by palladium (II) complex. Various metal enolates were screened, and tin(II) enolate gave the best result. Namely, the addition of $PdCl_2(CH_3CN)_2$ to the tin(II) enolate of 2-methyl-4-phenylbutane-2-one, generated in situ from stannous triflate and ketone in the presence of N-ethylpiperidine,[7)] afforded the corresponding α,β-unsaturated ketone in 54% yield. In the present reaction, oxo-π-allylpalladium decomposed to α,β-unsaturated ketone and palladium metal accompanied by generation of HCl, which was consumed to destroy tin(II) enolate. So, in order to raise the yield by trapping HCl, various acid captors were screened and diisopropylethylamine gave the best result. Furthermore, the yield was increased to 68% by the reverse addition, that is, the addition of tin(II) enolate solution to the mixture of $PdCl_2(CH_3CN)_2$ and diisopropylethylamine. Various α,β-unsaturated ketones were prepared from the corresponding saturated ketones as shown in Table 2.



(Scheme 2)

Table 2. Preparation of α,β-unsaturated ketones.

Entry	Ketone	Yield of 10 (%) [a]	Recovery of 9 (%)
1		78 (98) [b]	20
2		68 (75)	9
3		68 (88)	23
4		58 (72)	27
5	 $C_5H_{11}\overset{O}{\overset{\|}{C}}C_5H_{11}$ [c]	37 (74)	50
6		60 (72)	17

a) Isolated yields. All products gave satisfactory spectra data. (NMR and IR)
b) Yields in parenthese were based on consumed starting ketones.
c) KF and dibenzo-18-crown-6 were used as an acid captor.

A typical procedure for the preparation of 2-methyl-4-phenyl-2-butene-4-one was as follows: Under an argon atmosphere, to a methylene chloride (1 ml) suspension of stannous triflate (0.97 mmol) were added N-ethylpiperidine (1.1 mmol) and 2-methyl-4-phenylbutane-2-one (0.88 mmol) in methylene chloride (4 ml) at 0°C, and the reaction mixture was stirred for 15 min at this temperature, and then the suspended reaction mixture became a clear solution. This solution was added to a methylene chloride (6 ml) solution of $PdCl_2(CH_3CN)_2$ (0.89 mmol) and diisopropylethylamine (0.89 mmol) over 5 min at 0°C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Then aqueous solution of $NaHCO_3$ was added to the reaction mixture, and the insoluble materials were filtered off. The filtrate was extracted with methylene chloride and the organic layer was dried over Na_2SO_4. After removal of the solvent, the residue was purified by preparative TLC to give 2-methyl-4-phenyl-2-butene-4-one (0.60 mmol, 68%). The recovery of the starting ketone was 34 mg (0.21 mmol, 24%). There are several reports on the $PdCl_2$ catalyzed dehydrogenation reactions of saturated ketones to the corresponding α,β-unsaturated ketones,8) but the yield is generally low under rather severe reaction conditions. Compared with these methods, the present reaction proceeds smoothly to afford the corresponding α,β-unsaturated ketoens under mild conditions.

It is noted that, according to the present method, α,β-unsaturated aldehydes and ketones are conveniently prepared in fairly good yields by a one-pot procedure from the corresponding saturated carbonyl compounds.

References

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3) Silver trifluoromethanesulfonate was prepared according to the procedure of Whitesides and Gutowski. G. M. Whitesides and F. D. Gutowski, J. Org. Chem., 41, 2882 (1976).

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5) It has been reported that palladium tetrafluoroborate complex is generated in situ from dichloropalladium complex and two molar equivalents of silver tetrafluoroborate. M.-F. Hirai, M. Miyasaka, K. Ito, and Y. Ishii, J. Organometal. Chem., 165, 391 (1979).

6) Aldehyde 6 was prepared as follows: Ozone was bubbled into a methanol solution of 2-chloro-11-dodecene at -20°C for 2 h, and to the resulting solution was added a large excess of dimethylsulfide. The reaction mixture was warmed to room temperature, and stirred for 30 min. After removal of the solvent, aldehyde was distilled. Aldehydes 7 and 8 were also prepared by the same method.

6; bp 118°C/0.15 mmHg, NMR (CCl_4) δ=1.1 - 2.0 (m, 17 H), 2.1 - 2.5 (t, 2 H, 5 Hz), 3.9 (q, 1 H, 6 Hz), 9.6 (broad s, 1 H), IR (neat) 2700, 1720 cm^{-1}.

7; bp 126°C/1 mmHg, NMR (CCl_4) δ=1.0 - 2.0 (m, 17 H), 2.0 - 2.5 (m, 4 H), 4.0 (t, 2 H, 6 Hz), 9.6 (t, 1 H, 1 Hz), IR (neat) 1750, 1720 cm^{-1}.

8; bp 106°C/0.3 mmHg, NMR (CCl_4) δ=1.2 - 1.9 (m, 12 H), 2.0 (s, 3 H), 2.1 - 2.4 (m, 4 H), 9.6 (t, 1 H, 1 Hz), IR (neat) 2700, 1720 cm^{-1}.

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