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PALLADIUM-CATALYZED SYNTHESIS OF α,β-UNSATURATED KETONES FROM KETONES VIA ALLYL ENOL CARBONATES

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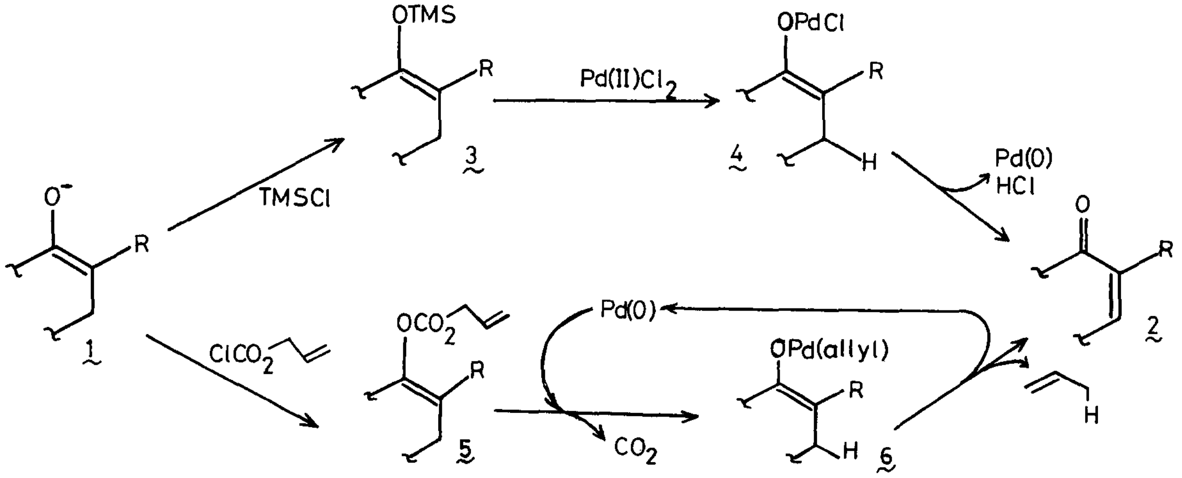
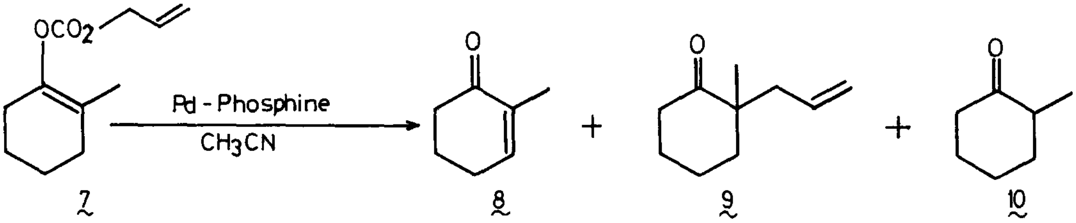
Summary: Allyl enol carbonates, prepared by quenching ketone enolates with allyl chloroformate, are converted to α,β-unsaturated ketones with $Pd(OAc)_2$-dppe catalyst in CH_3CN.

Regioselective introduction of α,β-unsaturation in unsymmetrical ketones is an important synthetic problem.1) As one method, direct oxidative dehydrogenation of saturated ketones to α,β-unsaturated ketones, promoted by Pd(II) salts, has been reported.2) But the conversion and selectivity are unsatisfactory. Enone formation was carried out regioselectively by the reaction of silyl enol ether with Pd(II) salts.3) In this reaction, the palladium enolate complex 4 is formed as an intermediate by the transmetallation of silyl enol ether with Pd(II) and then decomposed to the enone and Pd(0). The reaction requires cocatalyst to reoxidize Pd(0) for making the reaction catalytic. We expected that the enone formation from the enolates could be carried out catalytically if the palladium enolate complexes are prepared from Pd(0). As a related reaction, we obtained before α,β-unsaturated ketones by the palladium-catalyzed decarboxylation-dehydrogenation of allyl β-keto carboxylates.4) In this paper, we wish to report the palladium catalyzed synthesis of α,β-unsaturated carbonyl compounds via allyl enol carbonates.



Reaction of allyl enol carbonate 7 with Pd-phosphine catalyst to form the α,β-unsaturated ketone 8 was carried out under various conditions (Table 1). Careful selection of reaction conditions is necessary for efficient dehydrogenation. Especially ligands, solvents, and temperature play decisive roles. The enone 8 was obtained most selectively when the reaction was carried out at 80°C in CH_3CN in the presence of $Pd(OAc)_2$-1,2-bis(diphenylphosphino)ethane (dppe) (1 : 1) (run 2). Use of dppe as the bidentate ligand is essential. When the reaction was carried out at 20°C, allylation reaction took place to give 2-allyl-2-methylcyclohexanone (9) in 41% yield (run 1).[5] The ratio of $Pd(OAc)_2$ and dppe was important for the selective enone formation. When two equivalents of dppe were used, the allylated product 9 was obtained as a major product (run 4). In addition to dppe, 1,3-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb) were also good ligands for the enone synthesis. But when $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ was used instead of $Pd(OAc)_2$, the allylated product 9 was obtained in good yields. When the protic solvent such as *t*-BuOH was added, the selectivity of the enone formation decreased dramatically (run 3).

Table 1. Reaction of Allyl Enol Carbonate 7 with Pd Catalyst in CH_3CN[a)]

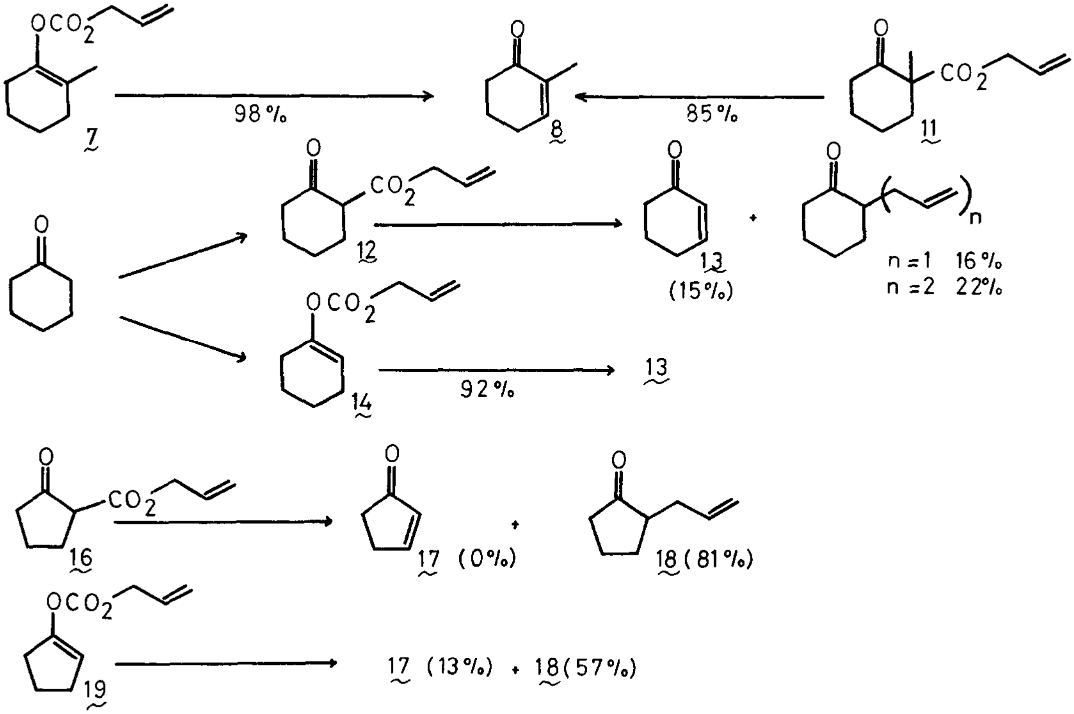


Run	Catalyst (ratio of Pd/Phosphine)		Yield(%)[b)] 8	9	10
1[c)]	$Pd(OAc)_2$-dppe	(1/1)	9	41	8
2			98	0	1
3[d)]			9	30	60
4		(1/2)	38	57	4
5		(2/1)	86	0	4
6	$Pd(OAc)_2$-PPh_3	(1/2)	69	18	10
7	$Pd(OAc)_2$-dppp[e)]	(1/1)	76	14	1
8	$Pd(OAc)_2$-dppb	(1/1)	80	0	9
9	$1/2Pd_2(dba)_3$ $CHCl_3$-dppe	(1/1)	5	95	0
10	$Pd(PPh_3)_4$-dppe	(1/1)	5	93	2

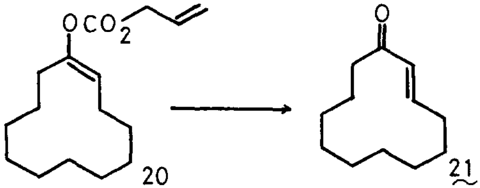
a) Reactions were carried out using Pd catalyst (0.1 mmol) and 7 (1 mmol) in dry CH_3CN (5 mL) at 80°C under argon for 1 h. b) GLC analysis. c) at 20°C for 24 h. d) *t*-BuOH (1 mL) was added. e) $Ph_2P(CH_2)_3PPh_2$. f) $Ph_2P(CH_2)_4PPh_2$.

Other allyl enol carbonates 14, 19, 20, and 22 were converted to α,β-unsaturated carbonyl compounds 13, 17, 21, and 23 respectively with $Pd(OAc)_2$-dppe catalyst in CH_3CN.

The enone 8 is also obtained selectively from allyl β-keto carboxylate 11 in the presence of Pd-dppe catalyst, as reported before.4) But the reaction of allyl β-keto carboxylate 12 which possesses an active hydrogen gave the allylated ketones as major products and the enone 13 was a minor product. Cyclopentenone (17) was not obtained from the allyl β-keto carboxylate 16, and 2-allylcyclopentanone (18) was a major product (81% yield). On the contrary, reaction of the enol carbonate 14 from cyclohexanone gave the enone 13 in 92% yield. Cyclopentenone (17) was obtained from allyl enol carbonate of cyclopentanone 19 in 13% yield, but the major product was the allylated product 18 (57% yield). The allylpalladium enolate complexes are expected to be formed from both allyl β-keto carboxylates and allyl enol carbonates. The allyl enol carbonates afford the enones more selectively than allyl β-keto carboxylates, especially in the case of α-unsubstituted cyclic ketones.



Only (*E*)-olefin 21 was obtained in 76% yield by the reaction of the allyl enol carbonate 20 prepared from cyclododecanone [NMR (CCl_4) δ 6.15 (d, *J* = 17 Hz, 1H, COCH=), 6.65 (dt, *J* = 17 and 6 Hz, 1H, CH=C$\underline{H}$-CH_2)]. Reaction of the allyl enol carbonate 22 prepared from cyclohexanecarboaldehyde gave the α,β-unsaturated aldehyde 23 in 90% yield.



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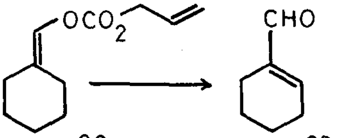

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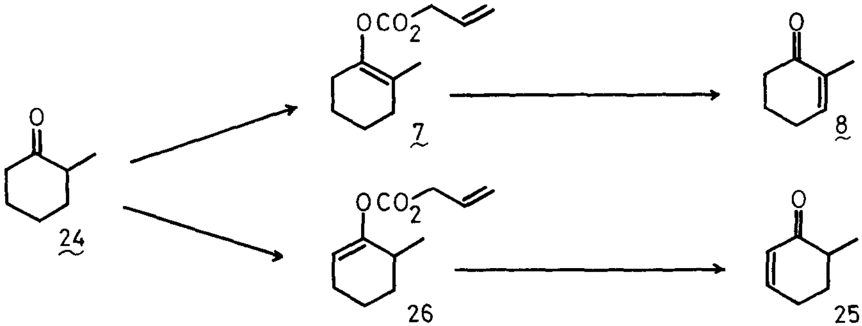
The reaction of allyl enol carbonates of unsymmetrical ketones is regioselective. As shown in Table 1, the reaction of the allyl enol carbonate 7 obtained from thermodynamically stable enolate of 23 gave 8 selectively. On the other hand, the allyl enol carbonate 26 obtained from kinetically generated enolate of 24 gave 6-methyl-2-cyclohexenone (25) in 81% yield. Thus, this is a good method for selective synthesis of α,β-unsaturated ketones from the selectively generated enolates.



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Further mechanistic studies and synthetic applications of this reaction are in progress.

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