

Synthesis of α,β -Unsaturated Carbonyl Compounds by Palladium(II)-Catalyzed Dehydrosilylation of Silyl Enol Ethers

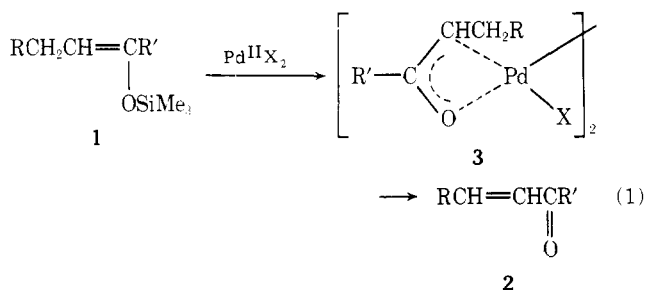
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α,β -Unsaturated carbonyl compounds are very versatile in organic syntheses, especially in the synthesis of steroidal natural products, and various methods for the introduction of the α,β carbon-carbon double bond to ketones and aldehydes have been explored.¹ One of the general approaches to α,β -unsaturated carbonyl compounds involves direct dehydrogenation of the corresponding saturated carbonyl compounds with strong oxidizing agents.² It has been reported that Pd^{II}Cl₂ catalyzes the dehydrogenation of saturated ketones to give the corresponding α,β -unsaturated ketones,^{2d-f} but the conversion in this direct dehydrogenation using Pd^{II}Cl₂ catalyst is generally low, and the products are complicated because of the lack of regioselectivity in the case of unsymmetrical ketones.

We have already reported a new synthesis of 1,4-diketones by the reaction of silyl enol ethers with Ag₂O, in which Ag(I) enolate intermediates are assumed.³ Herein, we wish to report a new and versatile method for the preparation of α,β -unsaturated carbonyl compounds (**2**) by the reaction of silyl enol ethers (**1**) with Pd^{II}(OAc)₂ in acetonitrile, in which an intermediate of the oxo- π -allylpalladium(II) complex (**3**)⁴ may be involved. An interesting feature of this reaction is the regioselective introduction of an α,β carbon-carbon double bond to unsymmetrical ketones via the corresponding silyl enol ethers as shown in eq 1.



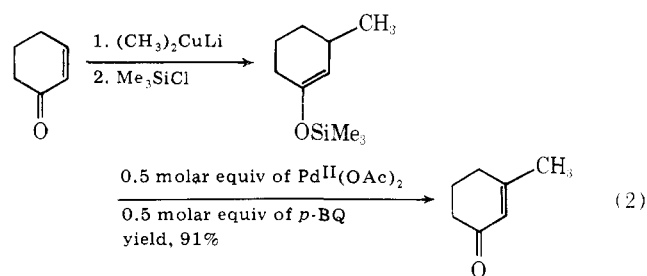
A general experimental procedure is illustrated as follows. To a stirring solution of Pd^{II}(OAc)₂ (0.5 mmol) and *p*-benzoquinone (0.5 mmol) in acetonitrile (4 mL), silyl enol ether (1.0 mmol) was added under nitrogen at room temperature, and then the resultant mixture was stirred for 2–30 h. Gas chromatography of the reaction mixture indicated that the desired α,β -unsaturated carbonyl compound **2** was produced in an excellent yield together with a few percent of the corresponding saturated carbonyl compound. The product of **2** was isolated by column chromatography on silica gel eluting with benzene and identified by comparison of its IR and NMR spectra with those of an authentic sample. Some results are summarized in Table I.

Use of a stoichiometric amount of Pd^{II}(OAc)₂ in the above reaction afforded a quantitative yield of the desired α,β -unsaturated carbonyl compound even in the absence of *p*-benzoquinone. Therefore, *p*-benzoquinone in the present reaction appears to function to regenerate an active Pd(II) species.^{2d} In fact, 1,4-bis(trimethylsilyloxy)benzene and *p*-trimethylsilyloxyphenol were isolated from the reaction mixture. When Pd^{II}(OAc)₂ was decreased to 0.25 molar equiv in the presence of 1.0 molar equiv of *p*-benzoquinone, however, the dehydrosilylation was decelerated remarkably, re-

sulting in a considerable decrease in the yield of α,β -unsaturated carbonyl compound **2** and an increase in the yield of the corresponding saturated carbonyl compound (run no. 3). Use of Pd^{II}Cl₂ instead of Pd^{II}(OAc)₂ produced a moderate yield of α,β -unsaturated carbonyl compound, being contaminated with a substantial amount of the saturated carbonyl compound (run no. 4). The less effectiveness of Pd^{II}Cl₂ may be due to the poor solubility of Pd^{II}Cl₂ in acetonitrile. The Pd^{II}Cl₂-(C₆H₅CN)₂ complex, which is soluble in benzene, furnished an improved result (run no. 5).

Regiospecificity of this reaction is illustrated by the dehydrosilylations with 2- (**1d**)⁵ and 6-methyl-1-trimethylsilyloxy-1-cyclohexene (**1e**) producing a 94% yield of 2-methyl-2-cyclohexenone (**2d**) and an 85% yield of 6-methyl-2-cyclohexenone (**2e**), respectively, without being contaminated with any isomeric cycloolefinic ketones (runs no. 7 and 8).

Furthermore, the combination of this dehydrosilylation with the preparation⁶ of silyl enol ethers from enolates, which were generated regioselectively by the conjugate addition of lithium dialkylcopper to α,β -unsaturated carbonyl compounds, makes the present synthesis of α,β -unsaturated carbonyl compounds more useful, as exemplified in eq 2.



Another important feature of the present reaction is the stereoselectivity of the olefin geometry of the α,β -unsaturated carbonyl compounds produced. The Pd^{II}(OAc)₂-induced dehydrosilylation of an *E* and *Z* mixture of 1-trimethylsilyloxy-1-cyclododecene (**1g**) produced selectively (*E*)-2-cyclododecenone (**2g**) in a 94% yield. Similarly, (*E*)-3-nonen-5-one (**2h**) and (*E*)-2-hexenal (**2i**) were produced selectively by the dehydrosilylations of an *E* and *Z* mixture of 5-trimethylsilyloxy-4-nonene (**1h**) and 1-trimethylsilyloxy-1-hexene (**1i**), respectively. No *Z* products have been observed.

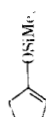














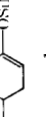


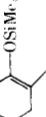


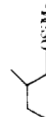


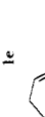


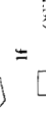





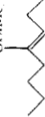


The Pd(II)-catalyzed dehydrosilylation in this study, which may be regarded as a reverse reaction of the transition-metal-induced 1,4-addition of hydrosilanes to α,β -unsaturated carbonyl compounds,⁷ is considered to involve the oxo- π -allylpalladium(II) complex (**3**)⁴ as a key intermediate. Actually, in the reaction of the silyl enol ether of acetophenone with Pd^{II}Cl₂ a stable oxo- π -allylpalladium(II) complex corresponding to **3** was isolated. Work is in progress to investigate a full scope of the synthesis of α,β -unsaturated carbonyl compounds and the chemistry of oxo- π -allylpalladium(II) complexes.

Experimental Section

Materials. Silyl enol ethers (**1**) were prepared from the corresponding ketones, aldehydes, and trimethylchlorosilane according to the reported procedure.⁸ 3-Methyl-1-trimethylsilyloxy-1-cyclohexene was prepared by the conjugate addition of lithium dimethylcopper to 2-cyclohexenone followed by treating with trimethylchlorosilane according to the reported procedure.⁶ Pd^{II}(OAc)₂ and Pd^{II}Cl₂ were commercial reagents. Pd^{II}Cl₂-(C₆H₅CN)₂ was prepared according to the reported procedure.⁹

Preparation of 2-Cyclohexenone by Pd^{II}(OAc)₂-Catalyzed Dehydrosilylation of 1-Trimethylsilyloxy-1-cyclohexene (1b**).** To a clear solution of 112 mg (0.5 mmol) of Pd^{II}(OAc)₂ and 54 mg (0.5 mmol) of *p*-benzoquinone in 4 mL of acetonitrile, 170 mg (1.0 mmol) of 1-trimethylsilyloxy-1-cyclohexene (**1b**) was added with stirring under nitrogen at room temperature, and then the mixture was stirred for 3 h. Gas chromatography of the reaction mixture indicated 2-

Table I. Preparation of α,β -Unsaturated Carbonyl Compounds by Pd(II)-Catalyzed Dehydroxylation of Silyl Enol Ethers^a

Run no.	Silyl enol ether 1	Registry no.	Pd(II) salt (equiv)	Registry no.	Reaction, h	Registry no.	Products (%) ^b	Registry no.
1		19980-43-9	Pd(OAc) ₂ (0.5)	3375-31-3	2	930-30-3	 (98),  (1)	120-92-3
2		6651-36-1	Pd(OAc) ₂ (0.5)		3	930-68-7	 (95),  (3)	108-94-1
3			Pd(OAc) ₂ ^c (0.25)		26		 (61),  (20)	
4			PdCl ₂ ^c (0.5)	7647-10-1	26		 (50),  (42)	
5			PdCl ₂ (PhCN) ₂ ^{c,d} (0.5)	14220-64-5	3		 (76),  (15)	
6		38671-78-2	Pd(OAc) ₂ (0.5)		5	5515-76-4	 (91),  (8)	589-92-4
7		19980-35-9	Pd(OAc) ₂ (0.5)		30	1121-18-2	 (94),  (5)	583-60-8
8		19980-33-7	Pd(OAc) ₂ (0.5)		5	6610-21-5	 (85),  (8)	
9		22081-48-7	Pd(OAc) ₂ (0.5)		2	1121-66-0	 (91),  (8)	502-42-1
10			Pd(OAc) ₂ (0.5)		4	6221-50-7	 (94),  (4)	830-13-7
11			Pd(OAc) ₂ (0.5)		3	52688-00-3	 (97),  (2)	502-56-7
12			Pd(OAc) ₂ (0.5)		3	6728-26-3	 (92),  (2)	66-25-1

^a Dehydroxylation was carried out by mixing 1.0 mmol of silyl enol ether and 0.5 mmol of Pd(OAc)₂ in 4 mL of acetonitrile in the presence of 0.5 mmol of *p*-benzoquinone at room temperature, unless otherwise stated. ^b Yields based on the starting silyl enol ether are determined by GLC. ^c An *E* and *Z* mixture. ^d Benzene (4 mL) was used instead of acetonitrile solvent.

cyclohexenone was produced in a 95% yield together with a 3% yield of cyclohexanone. 2-Cyclohexenone was isolated in about 85% yield by column chromatography on silica gel eluting with benzene.

$\text{Pd}^{\text{II}}(\text{OAc})_2$ -catalyzed dehydrosilylation of other silyl enol ethers (1) was similarly carried out. The reaction time is indicated in the Table I. Products of α,β -unsaturated carbonyl compounds were identified by comparison of their IR and NMR spectra with those of authentic samples. The stereochemistry of (*E*)-2-cyclododecenone (2g) and (*E*)-2-hexenal (2i) was convincingly confirmed by comparison of their IR and NMR spectra with those of authentic samples.¹⁰ The stereochemistry of (*E*)-3-nonen-5-one (2h) was determined by the NMR coupling constant ($J_{\text{H-H}} = 15.6$ Hz) of the olefinic protons.

Preparation of 2-Cyclohexenone by $\text{Pd}^{\text{II}}\text{Cl}_2-(\text{C}_6\text{H}_5\text{CN})_2$ -Catalyzed Dehydrosilylation of 1-Trimethylsilyloxy-1-cyclohexene (1b). A mixture of 54 mg (0.5 mmol) of *p*-benzoquinone and 192 mg (0.5 mmol) of $\text{Pd}^{\text{II}}\text{Cl}_2-(\text{C}_6\text{H}_5\text{CN})_2$ was dissolved in 4 mL of benzene with stirring. To the homogeneous solution, 170 mg (1.0 mmol) of 1-trimethylsilyloxy-1-cyclohexene (1b) was added, and then the reaction mixture was stirred at room temperature for 3 h. The product of 2-cyclohexenone was isolated by column chromatography on silica gel eluting with benzene.

Registry No.—(*Z*)-1g, 55314-46-0; (*E*)-1g, 55314-44-8; (*Z*)-1h, 64682-31-1; (*E*)-1h, 64682-32-2; (*Z*)-1i, 64728-30-9; (*E*)-1i, 64682-33-3.

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- The $\text{Pd}^{\text{II}}(\text{OAc})_2$ -catalyzed dehydrosilylation of 1d proceeded very slowly but gave a good yield of 2-methyl-2-cyclohexenone (2d) without loss of regioselectivity.
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Structure and Reactivity.¹ 2.

2-*tert*-Butyl-3-cyano-7-oxabicyclo[4.1.0]heptane Stereoisomers: Pseudoaxial *tert*-Butyl Conformer and Epoxidation Reaction Path

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The stereoselectivities of alkene epoxidations are sometimes rather difficult to rationalize;² for the two examples given in Figure 1, the inhibited syn attack is obviously related to steric hindrance, the cyano group being also rather bulky in syn-1,3 situations; the electrostatic interaction of this group may also play a part in this stereoselectivity.

When the cyano group is equatorial, no stereoselectivity

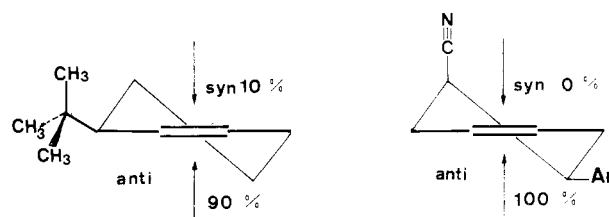


Figure 1. Induced stereoselectivities in the epoxidation of 3-*tert*-butylcyclohexene³ and 4-cyano-5-arylcylohexene.⁴

occurs: 50% of anti attack on *trans*-4-cyano-5-phenylcyclohexene in 1,2-dichloroethane as a solvent.⁴

Taking into account these results and the observed stereoselectivity for 4-cyanocyclohexene, 82 to 90% of anti attack,⁵ and also the conformational populations for this compound ($\Delta G^\circ \approx 0$),⁶ one can predict the ratio of the rates of anti attack ($k(a)$) on each conformer (a and e)

$$3.5 < (k_a(a)/k_e(a)) < 8$$

This result lacks in precision, but it shows a faster attack on the conformer with an axial cyano group. This analysis is based on the reasonable assumption, first made by Rickborn and Lwo,⁷ that the transition state conformation must be very similar to that of the starting alkene; the use of the ground state populations is then possible without violating the Curtin-Hammett principle.⁸

The problem of the epoxidation of *cis*- and *trans*-3-*tert*-butyl-4-cyanocyclohexenes must be also related to their conformational behavior:

(a) For the *cis* isomer, there is only one conformer at room temperature, the one with a pseudoequatorial *tert*-butyl group and an axial cyano substituent; the ring is in a half-chair conformation; this information has been established by NMR study⁹ and an x-ray crystal structure analysis.¹⁰

(b) For the *trans* isomer, NMR⁹ and vibrational¹¹ studies agree with two equally populated conformers.

(c) The "pseudoequatorial *tert*-butyl" conformer of this *trans* isomer has a *sofa* conformation similar to the one which has been determined in the crystallographic study of *trans*-1-acetoxy-3-*tert*-butyl-4-cyanocyclohexene;¹² the ring dihedral angles are $\phi_{12} = -4.3^\circ$, $\phi_{23} = -1.1^\circ$, $\phi_{34} = +29.4^\circ$, $\phi_{45} = -58.6^\circ$, $\phi_{56} = +53.3^\circ$, $\phi_{61} = -23.5^\circ$; the dihedral angle of the *tert*-butyl and the cyano C-C bonds is 86.5° .

(d) For the second conformer of the *trans* isomer ("pseudoaxial *tert*-butyl") we can reasonably expect another *sofa* conformation in which the axial character of the *tert*-butyl group would be less pronounced than in a half-chair conformation.

These conformational data are sufficiently uncommon to justify a study of the reactivity of these compounds; the epoxidation reaction is especially interesting owing to the relative simplicity of the reaction path (one-step reaction).

Results and Discussion

The epoxidation of *cis*-3,6,6-trideuterio-3-*tert*-butyl-4-cyanocyclohexene by *p*-nitroperbenzoic acid in chloroform gives only one compound 1, which is proved by gas chromatography and NMR spectroscopy. Except small differences in chemical shifts and in coupling constants, the NMR spectra of 1 and of its parent cyclohexene are quite identical.

The corresponding set of NMR parameters is reported in Table I. Long-range coupling constants (4J) are observed between each of the two bridgehead protons (H_1 and H_6) and a proton located near the cyano group (H_3 and H_4 , respectively); the difference between these two coupling constants is small but sufficient to allow the identification of transitions of protons H_1 and H_6 . The coupling between H_6 and one of the