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Palladium-Catalyzed Decarboxylative Allylic Alkylation of Allylic Acetates with β-Keto Acids

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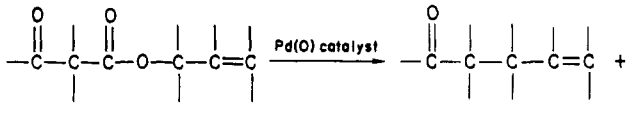
In the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium, β-keto acids react with allylic acetates at ambient temperature to produce α-allylic ketones in good yields with quantitative decarboxylation. This palladium-catalyzed decarboxylative allylic alkylation of allylic acetates with β-keto acids is characterized by high regio- and stereoselectivity. Allylation of β-keto acid takes place at the carbon atom bearing a carboxyl group. Allylic alkylation of allylic acetate with β-keto acid occurs at the less substituted end of the allyl group. The resultant carbon–carbon double bond of the α-allylic ketone has the *E* configuration. Allylic alkylation of lactone **25** with benzoylacetic acid proceeds preferably with retention of configuration, indicative of trans attack of the enolate on the (π-allyl)palladium intermediate from the opposite side of palladium even in the coexistence of free carboxylic acids.

Palladium-catalyzed allylic alkylation of allylic compounds with stabilized carbanions has recently been developed in organic synthesis.[1] Use of ketone enolate as a less stabilized nucleophile increases the potential of this type of allylic alkylation reaction, since chemoselective α-alkylation of ketone is an important synthetic transformation. Recently, we reported regioselective allylic alkylation with ketone enolates by palladium-catalyzed decarboxylation of allylic β-keto carboxylates (eq 1).[2] For

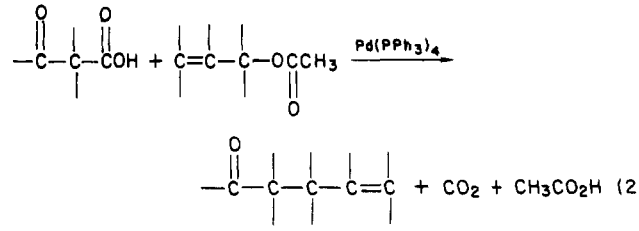


CO_2 (1)

the extension of the scope of this type of reaction and for the elucidation of its mechanistic questions, we have now studied the palladium-catalyzed reaction of β-keto acids and allylic acetates.

Results and Discussions

In the presence of 5 mol % of $Pd(PPh_3)_4$, β-keto acids were reacted with allylic acetates in benzene or tetrahydrofuran (THF) at room temperature to produce α-allylic ketones with quantitative evolution of CO_2 (eq 2). α-Allylic ketones are the allylic alkylation products of allylic acetates by β-keto acids. β-Keto acids employed



here were 1-oxocyclohexane-2-carboxylic acid (**1**), 6-methyl-1-oxocyclohexane-2-carboxylic acid, benzoylacetic acid, 1,3-acetonedicarboxylic acid (**2**), and 1-oxoindan-2-carboxylic acid. The results are summarized in Table I. α-Allylic ketones were produced efficiently under mild reaction conditions. The reaction is featured by high regio- and stereoselectivity. Allylation of 6-methyl-1-oxocyclohexane-2-carboxylic acid with allyl acetate occurred regioselectively at the carbon atom bearing a carboxyl group (entry 9). Concerning the reaction site on the allyl group, allylic alkylation of allylic acetates with β-keto acids also took place regioselectively at the less substituted allylic carbon atoms (entries 3, 4, 6, 7, 8).

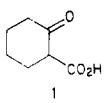
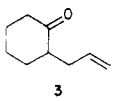
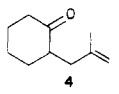
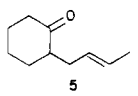
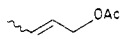
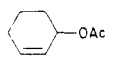
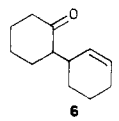
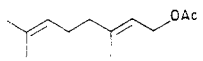
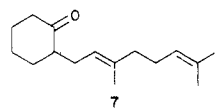
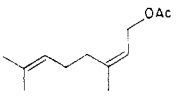
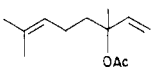
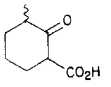
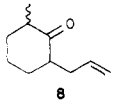
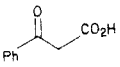
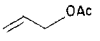
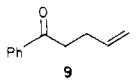
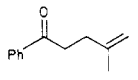
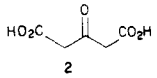
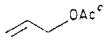
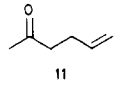
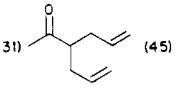
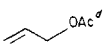
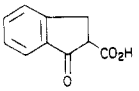
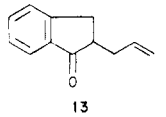
Stereochemistry of the resultant carbon–carbon double bond of α-allylic ketones was examined by the reaction of **1** with geranyl, neryl, and linalyl acetates. A single product of 2-geranylcyclohexanone (**7**) was obtained from these isomeric allylic acetates, which demonstrates *E* stereochemistry of the resultant carbon–carbon double bond (entries 6, 7, 8). The *E* stereochemistry of **7** was deduced from an upfield appearance of the ^{13}C NMR methyl signal on the basis of a shielding effect for a sterically compressed cis substituent (δ 16.07, Table IV, supplementary material).[3] Reaction of isomeric butenyl acetates and **1** also

(1) (a) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (b) Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer-Verlag: New York, 1980.

(2) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381–6384. See also: Simizu, I.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199–3202.

0022-3263/86/1951-0421$01.50/0

Table I. Palladium-Catalyzed Reaction of β-Keto Acids and Allylic Acetates[a]

entry	β-keto acid	allylic acetate	solvent	time (h)	α-allylic ketone	(yield, %)[b]	GLC analysis[e]
1	 1		C_6H_6	3	 3	(93)	A
2			THF	0.5	 4	(71)	A
3			THF	0.5	 5	(76)	A
4			THF	2	5	(84)	A
5			THF	20	 6	(49)	A
6			C_6H_6	5	 7	(78)	A
7			C_6H_6	5.5	7	(64)	A
8			C_6H_6	5	7	(83)	A
9			C_6H_6	1	 8	(94)	A
10			THF	1	 9	(89)	B
11			THF	0.5	 10	(74)	A
12	 2	 [c]	THF	0.5	 11 (31)  (45)		C
13		 [d]	THF	3	11 (64)	12 (5)	C
14			THF	0.5	 13	(70)	A

[a] All reactions were carried out under nitrogen using 1.00 mmol of β-keto acid, 1.00 mmol of allylic acetate, and 0.050 mmol of $Pd(PPh_3)_4$ in 5 mL of benzene or THF at ambient temperature. Quantitative CO_2 evolution occurred within the reaction time indicated. [b] Yield based on allylic ester was determined by GLC analysis. [c] 2.00 mmol of allyl acetate was used. Yield was based on **2**. [d] 4.00 mmol of **2** was used. [e] GLC analytical condition (column, internal standard): A (a silicone column, diphenyl ether), B (a silicone column, naphthalene), C (a PEG column, naphthalene).

produced a common main product of 2(*E*)-but-2-en-1-yl-cyclohexanone (**5**) (entries 3, 4). **5** showed its IR trans CH absorption at 970 cm^{-1}.

In the case of 1,3-acetonedicarboxylic acid (**2**) and allyl acetate, mono- and/or unsymmetrical diallylation products were obtained depending on reaction conditions. Use of an excess of **2** to allyl acetate produced predominantly the monoallylation product (**11**) (entry 13). Compound **11** is considered to be a product of the palladium-catalyzed reaction of allyl acetate with acetoacetic acid which is thermally unstable at room temperature for its preparation and manipulation. Thus, **2** may be used as an acetoacetic acid equivalent in the present reaction. Formation of a symmetrical diallylation product of 1,3-diallylacetone was not observed.

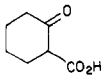
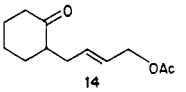
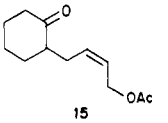
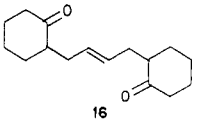
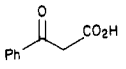
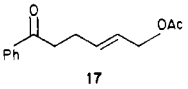
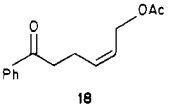
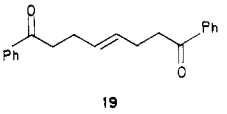
In addition to the palladium-catalyzed reaction of allylic β-keto carboxylates,[2] various methods for regio- and stereoselective allylic alkylation utilizing the attack of ketone enolates on (π-allyl)palladium complexes have recently been developed, i.e., palladium-catalyzed reaction of allyl enol carbonates[4] and palladium-catalyzed reaction of allylic acetates with lithium[5] and tin enolates.[6] Advantages of

(3) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730–4743.

(4) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 1793–1796.

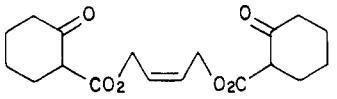
(5) Fiaud, J. C.; Malleron, J. L. *J. Chem. Soc., Chem. Commun.* **1981**, 1159–1160. See also: Abermark, B.; Jutand, A. *J. Organomet. Chem.* **1981**, *217*, C41–C43.

Table II. Palladium-Catalyzed Reaction of β-Keto Acids and (Z)-But-2-ene-1,4-diol Diacetate

entry	β-keto acid	AcO⁄⁄OAc	solvent	time (h)	products (yield, %)[b]		
					 14	 15	 16
15		1/6	C_6H_6	4	74	23	0
16		1/1	C_6H_6	4	39	10	17
17		2/1	C_6H_6	4	41	6	49
18		4/1[d]	C_6H_6	4	0	0	83
					 17	 18	 19
19		1/6	THF	2.5	53	27	0
20		4/1	THF	0.5	0	0	65[c]

[a] Reactions were carried out under nitrogen using 1 mmol of a minor component and 0.05 mmol of $Pd(PPh_3)_4$ in 5 mL of a solvent at ambient temperature. [b] Yield based on a minor component was determined by GLC analysis using a silicone column and phenanthrene as an internal standard except 19. [c] Isolated yield.

the present reaction using β-keto acids and allylic acetates over the previously developed reaction using allylic β-keto carboxylates (eq 1) are the ready availability of starting materials and the high yields of products. For example, palladium-catalyzed reaction of geranyl 1-oxocyclohexane-2-carboxylate produces **7** only in a yield of 39%[2] (cf. entry 6). Another merit of the present reaction is the easy control of allylic mono- and dialkylation of (Z)-but-2-ene-1,4-diol diacetate with β-keto acids by changing a feed ratio of two components. For example, the previously reported palladium-catalyzed reaction of (Z)-but-2-ene-1,4-diol bis(1-oxocyclohexane-2-carboxylate) (**21**) gives dialkylated product **16** in a moderate yield of 41%.[2]



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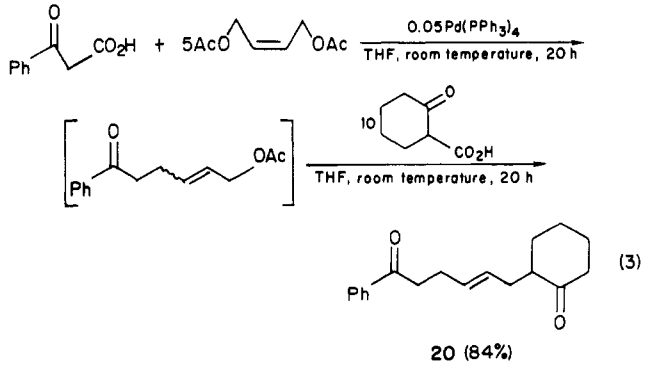
Efficient and selective allylic mono- and dialkylation of (Z)-but-2-ene-1,4-diol diacetate with β-keto acids can be effected, where the feed ratio of β-keto acids to the diacetate is crucial (Table II). Use of excess β-keto acid produced selectively a dialkylation product of symmetrical 1,8-diketone **16** or **19** in a good yield (entries 18, 20). On the contrary, use of excess diacetate gave selectively a monoalkylation product in a high yield (entries 15, 19). Unsymmetrical 1,8-diketone was obtained by successive treatment of the diacetate with two different β-keto acids without isolation of an intermediate monoalkylated product (eq 3). The *E* stereochemistry around the carbon–carbon double bonds of **14**, **15**, **17**, and **18** was assigned

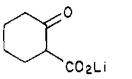
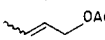
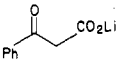
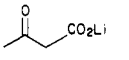
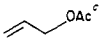
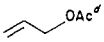


(3)

20 (84%)

(6) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2591–2594.

Table III. Palladium-Catalyzed Reaction of Lithium β-Keto Carboxylates and Allylic Acetates[a]

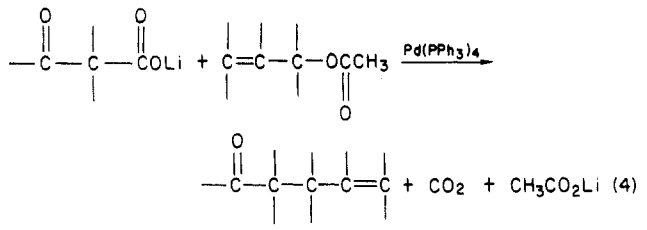
lithium β-keto carboxylate	allylic acetate	α-allylic ketone (yield, %)[e]
		**3** (92)
		**5** (80)
		**5** (85)
		**16** (67)
		**9** (77)
		**11** (14), **12** (64)
		**11** (55), **12** (10)

[a] All reaction were carried out under nitrogen using 1.00 mmol of lithium β-keto carboxylate, 1.00 mmol of allylic acetate, and 0.050 mmol of $Pd(PPh_3)_4$ in 5 mL of benzene at ambient temperature. Quantitative carbon dioxide evolution occurred within 1–3 h. [b] 4.00 mmol of (Z)-1,4-diacetoxybut-2-ene was used. [c] 3.33 mmol of allyl acetate was used. [d] 4.00 mmol of lithium acetoacetate and 5 mL of hexamethylphosphoric triamide were used. [e] Yield based on lithium β-keto carboxylate was determined by GLC analysis.

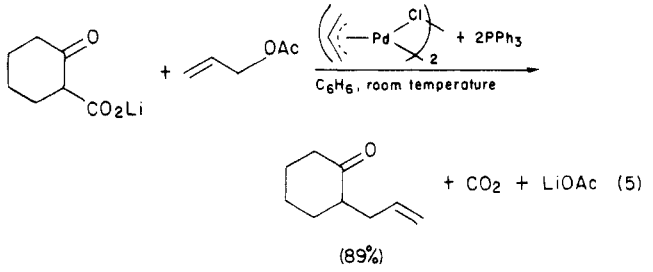
on the basis of the ^1H NMR chemical shifts of the methylene groups bearing an acetoxy moiety. Thus, the chemical shifts of the acetoxylated methylene groups with the *E* stereochemistry of **14** and **17** were δ 4.4–4.5. On the contrary, the methylene group having the *Z* configuration of **15** and **18** absorbed downfield at δ 5.1–5.4 due to a shielding effect for sterically compressed *Z* substituents. Similar quartet-like multiplets of *E* olefinic protons appeared at δ 5.1–5.9 in the ^1H NMR spectra of **14**, **16**, **17**, **19**, and **20**, which consistently showed IR CH absorptions of *E* olefins at 970 cm^{-1} (Table IV).

Control of monoallylation with allyl acetate is also possible. Previously reported palladium-catalyzed reaction of allyl acetoacetate is not selective and gives both allylacetone (37% yield) and 1,1-diallylacetone (16% yield).[2] On the other hand, the palladium-catalyzed reaction of allyl acetate with excess **2** produced allylacetone (**11**) in 64% yield with a small amount of 1,1-diallylacetone (**12**) (entry 13).

Instead of β-keto acids, lithium β-keto carboxylates were effective for allylic alkylation (eq 4). The efficiency of the reaction using lithium β-keto carboxylates is comparable to that of the reaction using β-keto acids. The results are



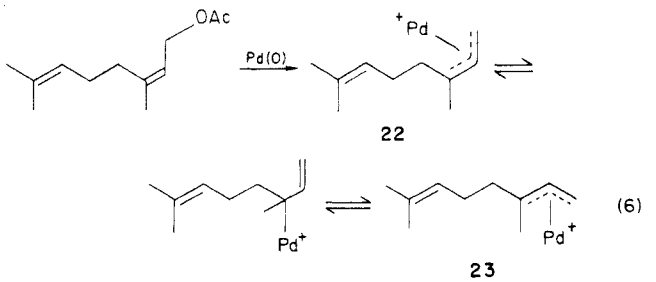
summarized in Table III. Sodium and potassium β-keto carboxylates were also effective. The higher stability of lithium β-keto carboxylates toward decarboxylation in comparison with the corresponding free β-keto acids permits ready availability of starting materials and facile manipulation for the present allylic alkylation reaction. (π-Allyl)palladium chloride in the presence of an added ligand acts as a catalyst for the allylic alkylation using lithium β-keto carboxylate (eq 5). Metathesis of these two



components produces the (π-allyl)palladium β-keto carboxylate intermediate which is involved in the catalytic cycle of Scheme I. (π-Allyl)palladium chloride catalyst may permit the use of a variety of ligands for the reaction.

The palladium-catalyzed reaction of 1 and allyl acetate as a representative may be understood by the assumed reaction path in Scheme I. Regioselective formation of α-allylic ketone suggests that the regioselectively generated enolate moiety holds its regiochemical integrity during the reaction. Formation of a single product from isomeric allylic acetates suggests intermediacy of a (π-allyl)palladium complex. Attack of enolate group onto the (π-allyl ligand at the less substituted allylic carbon atom leads to the observed regioselectivity.

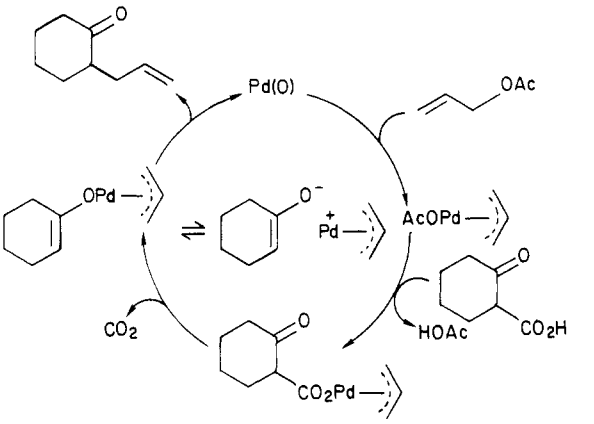
The *E* stereochemistry of the resultant carbon–carbon double bond indicates that the reaction proceeds via a syn (π-allyl)palladium complex. Complete reversal of olefin geometry in the allylic alkylation of neryl acetate shows that attack of the enolate group on the anti (π-allyl)palladium complex (**22**) is slower than its isomerization to the syn isomer (**23**). The isomerization involves conversion of the (π-allyl)palladium complex to the (σ-allyl)palladium complex and bond rotation (eq 6). The formation of **7**



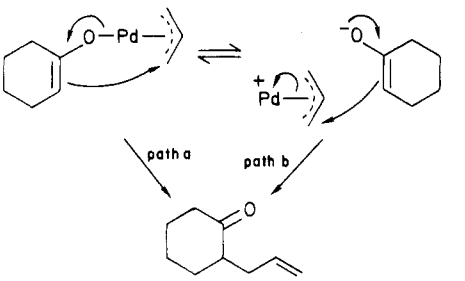
from neryl acetate makes a sharp contrast to the palladium-catalyzed reaction of neryl acetate with stabilized carbanions, where the stereochemistry of the trisubstituted double bond is retained.[3,7]

(7) Trost, B. M.; Verhoeven, T. R. *J. Org. Chem.* **1976**, *41*, 3215–3216.

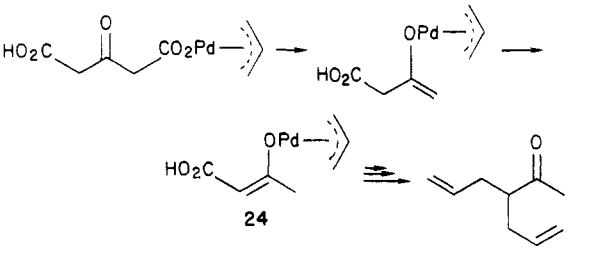
Scheme I



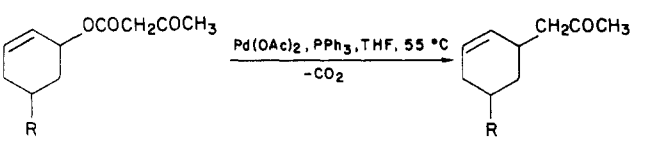
Scheme II



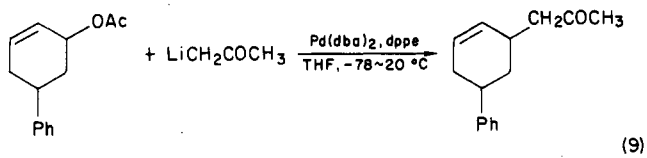
It is difficult to give a definite explanation of the formation of **11** and **12** in the reaction of **2** and allyl acetate. However, exclusive formation of unsymmetrical diallylacetone **12** without the symmetrical one suggests that isomerization of the firstly generated (π-allyl)palladium enolate complex to the more stable one (**24**) plays an important role in the reaction (eq 7).



The intriguing question in Scheme I concerns the mechanism of the coupling reaction between the enolate moiety and the π-allyl group, for which two paths a and b are possible (Scheme II). Path a involves intramolecular cis-migration of the enolate group from the coordination sphere of palladium. Path b proceeds via intermolecular nucleophilic trans attack of the enolate anion on the π-allyl group from the opposite side of palladium. In other words, the free enolate anion displaces the palladium with inversion of configuration. Discrimination of paths a and b by examining the stereochemistry of allylic alkylation with the enolate anion is a recent subject of discussion. Fiaud et al. have shown that the palladium-catalyzed allylic alkylation of (*Z*)-5-substituted-cyclohex-2-enyl acetoacetates proceeds with the overall retention of configuration (eq 8).[8] Bäckvall et al. have obtained the same results



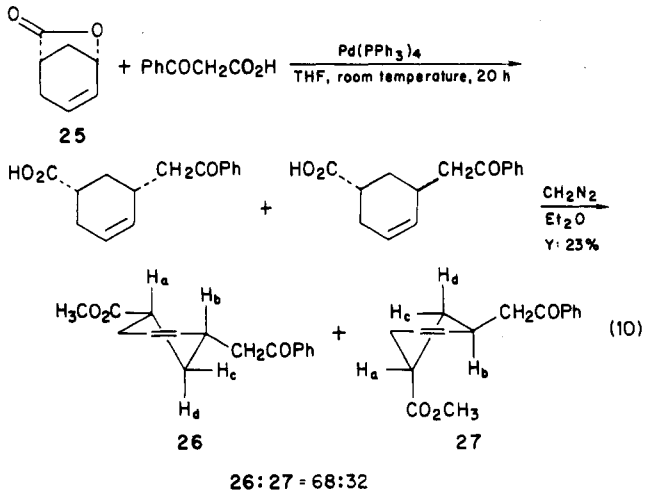
in similar reactions.[9] In addition, palladium-catalyzed allylic alkylation of (*Z*)-5-substituted-cyclohex-2-enyl acetates with preformed lithium[5] and tin[6] enolates also occurs stereospecifically with retention of configuration, for example, eq 9. As displacement of an acetate moiety



(9)

of allylic acetate by the palladium is accepted to occur with inversion of configuration,[3,10] these stereochemical results indicate that the enolate ion reacts via path b to substitute the palladium with inversion of configuration[5,6,8,9] as also found for stabilized carbanions.[3,11]

These findings suggest that the palladium-catalyzed reaction of β-keto acids and allylic acetates also takes place via path b. In the present reaction, however, free carboxylic acids, β-keto acid and acetic acid, exist in the reaction mixture. According to Scheme I, acetic acid is liberated in the amount of β-keto acid consumed, and the total amount of free carboxylic acids is kept constant throughout the reaction. The maximum ratio of free carboxylic acids to the enolate ion is 20 in the reaction using 5 mol % $Pd(PPh_3)_4$. Thus, it is interesting to examine whether path b involving the free enolate ion takes place even in the presence of free carboxylic acids which possibly destroy the enolate ion. The reaction of benzoylacetic acid and lactone **25** was carried out, which gave preferentially (*Z*)-3-(benzoylmethyl)-5-carbomethoxycyclohex-1-ene (**26**) over a corresponding *E* isomer (**27**) after treatment with CH_2N_2 (eq 10). Similarly, the re-

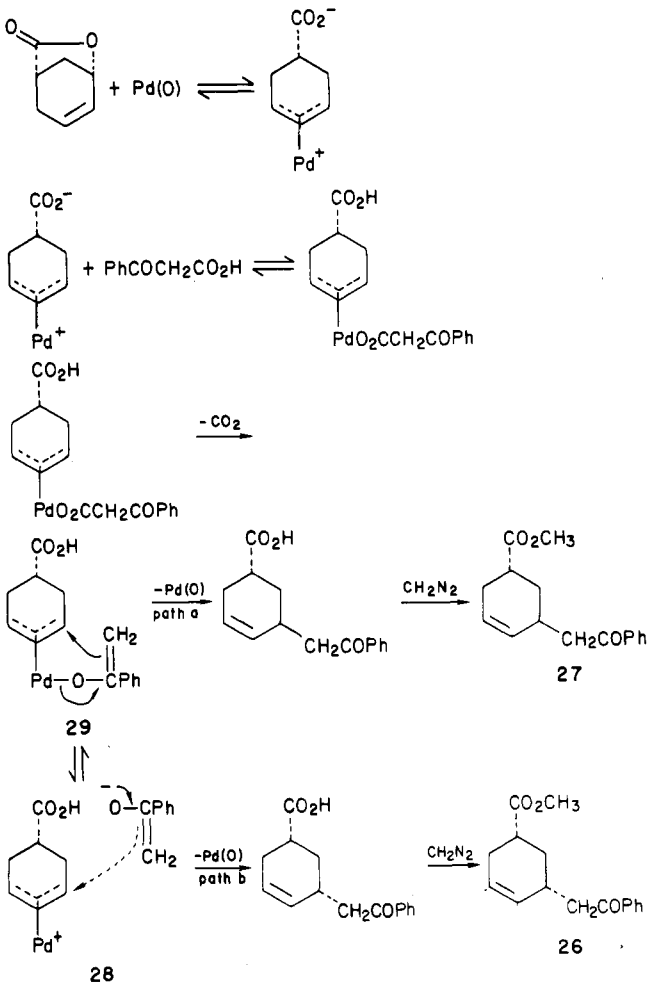


(10)

26:27 = 68:32

action in dimethylformamide produced **26** preferably in a ratio of **26:27** = 79:21. The *Z* and *E* stereochemistry of **26** and **27**, respectively, was easily determined by 300-MHz ^1H NMR spectroscopy.[3] The splitting of Hd (δ 1.34, d of t ≃ q, J_{cd} = 10.8, J_{ad} = J_{bd} = 12.6) of **26** clearly shows a pseudoaxial position of both Ha and Hb. On the other hand, the values of Hd (δ 1.99, d of d of d, J_{ad} = 5.7, J_{bd} = 10.5, J_{cd} = 13.3) and Hc (δ 1.81, d of t, J_{ac} = J_{bc} = 3.3, J_{cd} = 13.5) of **27** indicate that Ha is pseudoequatorial and Hb is pseudoaxial.

Scheme III



As is shown in Scheme III, the preferable formation of the *Z* isomer **26** is compatible with path b where the free acetophenone enolate anion makes a trans attack on the (π-allyl)palladium intermediate from the opposite side of the palladium. This stereochemical result suggests that the present palladium-catalyzed decarboxylative allylic alkylation of allylic acetates with β-keto acids proceeds in general via path b of Scheme II. As is described previously, however, the large amount of the free carboxylic acids of β-keto acid and acetic acid which may destroy the enolate anion are present in the reaction mixture. Thus, the above stereochemical conclusion necessitates the assumption that the free enolate anion reacts more rapidly with the (π-allyl)palladium intermediate than it reacts with the carboxylic acids. This assumption is not self-evident. Although there is no definite answer to this question at the present time, it is significant that the stereochemical result obtained here suggests a more complex nature of the coupling reaction of the enolate group and the (π-allyl)-palladium intermediate. The coupling might take place in an associated form of the (π-allyl)palladium enolate complex and the (π-allyl)palladium β-keto carboxylate complex without the participation of the free enolate anion. The low stereospecificity of the reaction of lactone **25** and benzoylacetic acid cannot be explained reasonably at the present time. The structure of lactone **25** excludes the possibility of palladium-assisted epimerization of the starting allylic acetate.[12] Epimerization of the (π-allyl)-palladium complex **28** might take place.[13] The low yield

(8) Fiaud, J. C.; Zouioueche, L. A. *Tetrahedron Lett.* **1982**, *23*, 5279–5282.
(9) Bäckvall, J. E.; Nordberg, R. E.; Vagberg, J. *Tetrahedron Lett.* **1983**, *24*, 411–412.
(10) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767–7768.
(11) Hayashi, T.; Konishi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1984**, 107–108.
(12) Trost, B. M.; Verhoeven, T. R.; Fortunak, T. M. *Tetrahedron Lett.* **1979**, 2301–2304.

of the allylic alkylation products **26** and **27** might result from the side elimination reaction of intermediate (π-allyl)palladium complexes to a 1,3-diene.[12]

Experimental Section

IR spectra were determined on a Hitachi 260-50 grating spectrophotometer. ^{1}H NMR spectra were taken on a Hitachi R-20B spectrometer. ^{13}C NMR were obtained on a Hitachi R-100. All chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Coupling constants are reported in hertz. Mass spectra were obtained on a JEOL D-300 instrument. Microanalyses were performed by the Microanalysis Center of Kyoto University. Gas chromatographic analyses (GLC) were made on a Shimadzu 4APT instrument. GLC quantitative analyses of reaction products were made with internal standards with calibration based upon authentic samples and by employing a 20% silicone DC 550 on Celite 545 column or a 20% polyethylene glycol (PEG) 20M on Celite 545 column. Carbon dioxide gas was analyzed by GLC on an activated charcoal column using methane as an internal standard.

Reactions were carried out under an atmosphere of nitrogen. Organic solvents were distilled from calcium hydride under nitrogen. Crotyl acetate, methallyl acetate, and cyclohex-2-enyl acetate were prepared by general methods using the corresponding allylic alcohols and acetyl chloride. The lactone **25** was prepared according to a published method.[14] Other allylic acetates were commercial reagents and were distilled from Drierite under nitrogen. β-Keto acids were prepared by the reported procedure[15] except **2** which was a commercial reagent. Lithium β-keto carboxylates were prepared similarly according to the preparative method of cuprous β-keto carboxylates.[16] Tetrakis(triphenylphosphine)palladium was prepared by the known method.[17] (π-Allyl)palladium chloride was prepared according to the published method.[18]

General Experimental Procedure for Palladium-Catalyzed Reaction of β-Keto Acids and Allylic Acetates. Reaction of 1 and Allyl Acetate as a Representative Procedure. To a stirred solution of **1** (0.1422 g, 1.00 mmol) and $Pd(PPh_3)_4$ (0.0578 g, 0.050 mmol) in 5 mL of benzene in a 200-mL flask equipped with a rubber septum and a three-way stopcock were added allyl acetate (0.104 mL, 1.00 mmol) using a microsyringe through the three-way stopcock under a countercurrent stream of nitrogen and subsequently methane gas (20.2 mL, 0.831 mmol) using a hypodermic syringe through the rubber septum. The reaction mixture was stirred at ambient temperature. Carbon dioxide gas evolution was monitored by GLC analysis of a gaseous sample taken out through the rubber septum with a hypodermic syringe. Quantitative carbon dioxide gas evolution was observed after 3 h. Addition of diphenyl ether (0.079 mL, 0.50 mmol) as a GLC internal standard and subsequent GLC analysis (a silicone DC 550 column) showed formation of **3** in 93% yield. **3** was isolated by GLC and identified by its IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data (Table IV).

Reaction of Benzoylacetic Acid and (*Z*)-But-2-ene-1,4-diol Diacetate. Following the above-mentioned usual procedure, a mixture of benzoylacetic acid (0.6568 g, 4.00 mmol), (*Z*)-but-2-ene-1,4-diol diacetate (0.158 mL, 1.00 mmol), and $Pd(PPh_3)_4$ (0.0578 g, 0.050 mmol) in 5 mL of THF was stirred at ambient temperature for 0.5 h. A resulting white precipitate was filtered, washed with a small amount of THF, and dried in vacuo to give **19** (0.190 g, 0.649 mmol, 65% yield). GLC analysis (a silicone DC 550 column) of the filtrate combined with the washing revealed no formation of **17** and **18**.

Synthesis of Unsymmetrical 1,8-Diketone 21. Benzoylacetic acid (0.6568 g, 4.00 mmol), (*Z*)-but-2-ene-1,4-diol diacetate (3.16 mL, 20 mmol), and $Pd(PPh_3)_4$ (0.2312 g, 0.200 mmol) were reacted in 20 mL of THF at ambient temperature for 20 h. **1** (5.688 g, 40.0 mmol) was added and the resulting reaction mixture was further stirred for 20 h. GLC analysis (a silicone DC 550 column, phenanthrene as an internal standard) showed formation of **21** in 84% yield.

Reaction of Lactone 25 and Benzoylacetic Acid. Benzoylacetic acid (1.4778 g, 9.00 mmol), **25** (0.624 mL, 6.00 mmol), and $Pd(PPh_3)_4$ (0.3468 g, 0.300 mmol) were reacted in 20 mL of THF at ambient temperature for 20 h. The reaction mixture was diluted with 10% aqueous hydrochloric acid, extracted with ether, and dried over anhydrous magnesium sulfate. The ether solution was treated with an ether solution of diazomethane generated in situ from *N*-methyl-*N*-nitrosourea (1.55 g, 15.0 mmol).[19] After 1 h, the excess diazomethane was quenched with acetic acid and subsequently the excess acetic acid was neutralized with aqueous sodium hydrogen carbonate. The ethereal organic layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated by evaporation in vacuo. Addition of phenanthrene (0.0891 g, 0.500 mmol) as an internal standard and GLC analysis (a 10% diethylene glycol succinate polyester on Neopak 1A column) indicated formation of **26** and **27** (**26**:**27** = 68:32) in 23% yield. Isolation of **26** and **27** was done by preparative TLC (Merck silica gel $60F_{254}$, benzene). ^{1}H NMR spectra of **26** and **27** was obtained on a Nicolet NT-300 spectrometer. **26**: IR (liquid film, cm^{-1}) 1735, 1690. ^{1}H NMR (300-MHz, $CDCl_3$, δ) 1.34 (d of t $\simeq$ q, J = 12.6, 10.8 Hz, 1 H), 2.15–2.35 (m, 3 H), 2.66 (m, 1 H), 2.96 (br s, 3 H), 3.68 (s, 3 H), 5.58 (d, J = 10.2 Hz, 1 H), 5.71 (m, 1 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.57 (t, J = 7.2 Hz, 1 H), 7.95 (d, J = 7.2 Hz, 2 H); mass spectrum, M$^+$ at m/e 258. **27**: IR (liquid film, cm^{-1}) 1735, 1690; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 1.81 (d of t, J = 13.5, 3.3 Hz, 1 H), 1.99 (d of d of d, J = 13.3, 10.5, 5.7 Hz, 1 H), 2.29 (m, 2 H), 2.65 (m, 1 H), 2.95–3.10 (m, 3 H), 3.68 (s, 3 H), 5.56–5.85 (m, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.57 (t, J = 7.2 Hz, 1 H), 7.96 (d, J = 7.2 Hz, 2 H); mass spectrum, M$^+$ at m/e 258.

Acknowledgment. We thank Professor B. M. Trost at the University of Wisconsin for helpful suggestions on the stereochemical experiment on the lactone **25**. This work was supported in part by Grant-in Aid for Scientific Research 60550588 from the Ministry of Education, Science, and Culture of Japan.

Registry No. **1**, 18709-01-8; 1·Li, 99706-17-9; **2**, 542-05-2; **3**, 94-66-6; **4**, 936-67-4; **5**, 72128-69-9; **6**, 18956-05-3; **7**, 74016-20-9; **8**, 36321-95-6; **9**, 3240-29-7; **10**, 1078-36-0; **11**, 109-49-9; **12**, 75265-80-4; **13**, 99706-09-9; **14**, 99706-13-5; **15**, 99706-14-6; **16**, 75265-79-1; **17**, 99706-15-7; **18**, 99706-16-8; **19**, 99706-10-2; **21**, 75265-75-7; **25**, 4720-83-6; **26**, 99706-11-3; **27**, 99706-12-4; $PhCOCH_2CO_2H$, 614-20-0; $PhCOCH_2CO_2Li$, 49714-69-4; $H_2C{=}CHCH_2OAc$, 591-87-7; $H_2C{=}C(CH_3)CH_2OAc$, 820-71-3; $H_2C{=}CHCH(CH_3)OAc$, 6737-11-7; (*E*)-$H_3CCH{=}CHCH_2OAc$, 7204-29-7; (*Z*)-$H_3CCH{=}CHCH_2OAc$, 7204-36-6; (*E*)-$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OAc$, 105-87-3; (*Z*)-$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OAc$, 141-12-8; $(CH_3)_2C{=}CH(CH_2)_2C(CH_3)(OAc)C{-}H{=}CH_2$, 115-95-7; $Pd(PPh_3)_4$, 14221-01-3; 3-methyl-2-oxocyclohexanecarboxylic acid, 25260-60-0; $H_3CCOCH_2CO_2Li$, 3483-11-2; 3-methyl-2-oxocyclohexanecarboxylic acid, 52456-87-8; 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylic acid, 6742-29-6; 2-cyclohexen-1-yl acetate, 14447-34-8.

Supplementary Material Available: Table IV, spectral data for ketones **3–20** (2 pages). Ordering information is given on any current masthead page.

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