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Stereochemical Study on the Palladium(0)-Catalyzed Carbonylation of 3-(Methoxycarbonyloxy)-2-methylenealkanoates and Analogues

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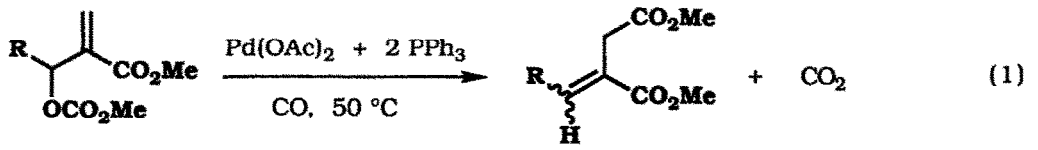
Key Words: palladium(0) complex; carbonylation; π-allylpalladium complex; the Baylis-Hillman reaction; stereochemistry

Abstract: *A series of 3-(alkoxycarbonyloxy)-2-methylenealkanoate (1), a sulfonate (5), and an N,N-dimethylamide (6) were carbonylated using Pd(0) complexes as catalyst to give alkylidenesuccinate (2), and analogues in moderate to good yields. The stereoselectivity for E and Z isomers of carbonylation products was found to differ remarkably, depending on the three types of substrates which always include an electron-withdrawing group. The results are explained in terms of the plausible MM2 simulation through the model compounds.*

It has been reported by Tsuji et al.[1] that allylic carbonates are very susceptible to oxidative addition to Pd(0) species, undergoing facile decarboxylative carbonylation to give β,γ-unsaturated esters under mild conditions.[2,3] Their procedure appears to occupy a prominent place among a variety of Pd(0)-catalyzed carbonylations of allylic substrates due to its facility.

We have been concerned with the Pd(0)-catalyzed, regioselective carbonylation of 3-(methoxycarbonyloxy)-2-methylenealkanoates (**1**) to give predominantly (*E*)-alkylidenesuccinates (**2**),[4] (eq. 1). It was



(1)

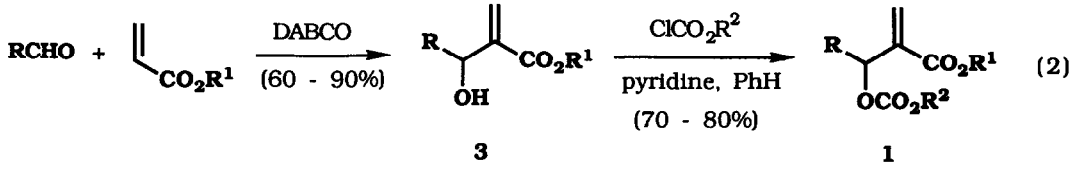
1 **2**

also found that the carbonylation of the cyano analogue of **1** afforded mainly (*Z*)-3-cyano-3-alkenoate, reflecting presumably the *syn*-alkyl-π-allylpalladium intermediate to be carbonylated preferably.[4] The reaction involves an interesting issue of remarkable difference in steric effects between two electron-withdrawing groups (EWG), which occupy the 2-position of 1,2-disubstituted π-allylpalladium intermediates. To our best knowledge, few studies are reported on the Pd(0)-mediated reactions regarding these intermediates, which involves the allylation of dimethyl sodiomalonate in a rather non-stereoselective manner.[5] Accordingly, we have undertaken an extensive study on the Pd(0)-catalyzed carbonylation of these types of allylic carbonates. We report here the Pd(0)-catalyzed carbonylation of 3-(methoxycarbonyloxy)-2-methylenealkanoates (**1**) and analogues in order to look at the stereochemical outcome of the carbonylation products which may reflect the geometry of 1,2-disubstituted π-allylpalladium intermediates.

RESULTS AND DISCUSSION

a) *Preparation of 3-(methoxycarbonyloxy)-2-methylenealkanoates (**1a-h**), a sulfonate (**5**), and an N,N-dimethylamide (**6**).*

(i) In order to extend the scope of the regio- and stereoselective carbonylation of **1** (R = *i*-Bu),[4] we have prepared a series of 3-(methoxycarbonyloxy)-2-methylenealkanoate (**1a-1h**) according to a two-step procedure which consists of a base-catalyzed addition of acrylates to aliphatic aldehydes (the Baylis-Hillman reaction)[6] followed by the carbonate formation of the resulting allylic alcohols (**3**), (eq. 2). The Baylis-Hillman reaction of



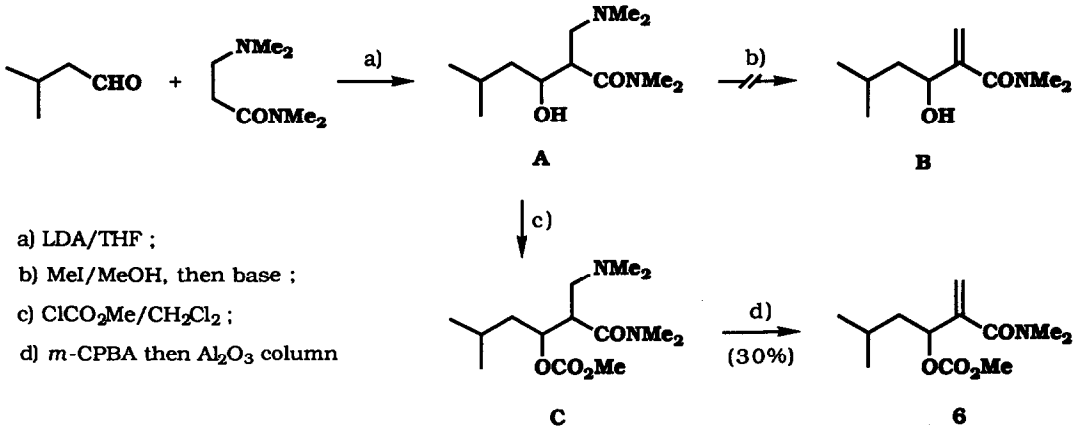
(2)

an acrylate was carried out using an excess aldehyde (1.5-2 equiv) in the presence of either 1,4-diazabicyclo[2.2.2]octane (DABCO; 20 mol%) or 3-quinuclidinol (10 mol%)[7] to give, usually in a week, 3-hydroxy-2-methylenealkanoate (**3**) in 60-90% yields.

(ii) The similar reaction of phenyl ethylenesulfonate with 3-methylbutanal proceeded very rapidly (3 h) in benzene solution, giving phenyl 3-hydroxy-5-methyl-1-hexene-2-sulfonate (**4**) in 87% yield. Carbonate formation of **4** required rather forcing conditions using $ClCO_2Et$ and NaH in the presence of a catalytic amount of dicyclohexano-18-crown-6 in ether under refluxing for two weeks and phenyl 3-(ethoxycarbonyloxy)-5-methyl-1-hexene-2-sulfonate (**5**) was obtained in 71% yield.

(iii) Although there has been a report that acrylamide undergoes a base-catalyzed addition to an aldehyde under high pressure,[8] the Baylis-Hillman reaction of *N,N*-dimethylacrylamide with 3-methylbutanal entirely failed. The requisite 3-hydroxy-5-methyl-2-methylene-*N,N*-dimethylhexanamide (**B**) was also found to be hardly

prepared even by an indirect procedure[9] using 3-(*N,N*-dimethylamino)-*N,N*-dimethylpropanamide as depicted in Scheme 1. Thus, attempted Hofmann elimination after quaternization of 2-(*N,N*-dimethylaminomethyl)-3-hydroxy-5-methyl-*N,N*-dimethylhexanamide (**A**) did not take place, but resulted exclusively in giving *N,N*-dimethylacrylamide *via* the retro-aldol reaction. It was eventually found that 2-(*N,N*-dimethylaminomethyl)-3-(methoxycarbonyloxy)-5-methyl-*N,N*-dimethylhexanamide (**C**), obtained by a carbonate formation from **A**, underwent smooth β-elimination of an *N*-oxide[10] to give 3-(methoxycarbonyloxy)-5-methyl-2-methylene-*N,N*-dimethylhexanamide (**6**) in a moderate yield.



Scheme 1

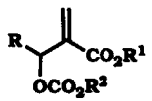
All 3-(alkoxycarbonyloxy)-2-methylenealkanoate (**1a-h**), a sulfonate (**5**), and an *N,N*-dimethylamide (**6**) analogue thus prepared are listed in Table I including their spectral data.

b) *Palladium(0)-catalyzed carbonylation of 3-(methoxycarbonyloxy)-2-methylenealkanoates (1) and analogues.*

The decarboxylation-carbonylation was carried out using **1a-h** in the presence of a catalytic amount (2 mol%) of a palladium(0)-phosphine complex, usually generated *in situ* from $Pd(OAc)_2$ + 2 PPh_3, under carbon monoxide pressure (20 atm) at 50 °C for 15 h as the most reliable conditions (eq. 1). The carbonylation of **1** proceeded straightforward to give the corresponding alkylidenesuccinates (**2**) in moderate to good yields. The regioselective carbonylation of **1** always retained but the stereoselectivity for *E* and *Z* isomers of **2** and yields deteriorated significantly under CO pressure less than 20 atm as reported previously.[4] In Table II are summarized the results of Pd(0)-catalyzed carbonylation of **1** and the selectivity for *E/Z* isomers of **2**.

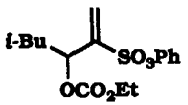
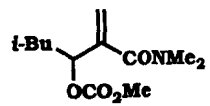
It is evident from Table II that the carbonylation of **1** containing a variety of R (originated from aldehydes) and R^1 (from acrylates) gave rise uniformly to (*E*)-alkylidenesuccinate **2** as a major product with 90-93% selectivity. Introduction of bulky substituents, such as R=*i*-Pr (Entry 6) and R^1=*t*-Bu (Entries 3,5, and 9), to the substrate **1** is expected to improve the stereoselectivity for *E/Z* isomers of product **2**, provided that 1,2-

Table I. Spectral Data for 3-(Methoxycarbonyloxy)-2-methylenealkanoate (**1**), a Sulfonate (**5**), and an *N,N*-Dimethylamide (**6**)



R	R^1	R^2	Entry	Yield(%)[a]	^{1}H NMR($CDCl_3$,TMS), δ	^{13}C NMR, δ	IR(cm^{-1})	MS(EI or CI)
Me	Me	Me	**1a**	9[b]	1.46(d, *J*=6.4 Hz), 3.79(s), 5.59(q, *J*= 6.4 Hz), 5.88(s), 6.32(s)	20.3, 52.0, 54.7, 72.1, 125.0, 140.7, 154.8, 165.5	1744, 1728, 1633, 791	156 (M^+ -MeOH)
Me	Et	Et[c]	**1b**	92	1.31(t, *J*=7.2 Hz), 1.46(d, *J*=6.4 Hz), 4.20(q, *J*=7 Hz), 4.24(q, *J*=7 Hz), 5.60(q, *J*=6.4 Hz), 5.87(s), 6.31(s)	14.1, 14.2, 20.3, 60.9, 64.0, 71.8, 124.6, 141.1, 154.2, 165.1	1745, 1729 1633, 791	170 (M^+ -EtOH)
Me	*t*-Bu	Me	**1c**	68	1.44(d, *J*=6.4 Hz), 1.50(s), 3.78(s) 5.57(br q), 5.78(s), 6.22(s)	20.2, 28.0, 54.6, 72.1, 81.3 123.6, 142.3, 154.8, 164.2	1752, 1719 1634, 792	174 (M^+ -isobutene)
Et	*t*-Bu	Me	**1d**	75	0.94(t, *J*=7 Hz), 1.50(s), 1.75(m), 3.78(s), 5.42(br t), 5.73(s), 6.23(s)	9.2, 27.2, 27.7, 54.2, 76.6, 80.8, 123.6, 141.0, 154.8, 164.1	1752, 1713, 1632, 793	188 (M^+ -isobutane)
i-Pr	Me	Me	**1e**[d]	40[e]	0.92(d, *J*=6.6 Hz), 0.96(d, *J*=6.8 Hz), 2.02(m), 3.78(s), 3.79(s), 5.34(dd, *J*=0.9, 5.5 Hz), 5.80(t, *J*=1.0 Hz), 6.30(d, *J*=0.9 Hz)	16.9, 18.8, 31.6, 52.0, 54.8, 80.0, 126.2, 139.1, 155.2, 165.7	1750, 1720, 1634	——
i-Bu	Me	Me	**1f**[d]	85	0.93(d, *J*=5.9 Hz), 0.96(d, *J*=5.7 Hz), 1.59(m), 3.78(s), 3.79(s), 5.52(m), 5,84(br s), 6.30(br s)	21.7, 23.1, 24.9, 43.9, 52.0, 54.8, 74.4, 125.1, 140.6, 155.1, 165.6	1750, 1720, 1632	——

Table I. (Continued)

i-Bu	*i*-Pr	Me	**1g**[d]	70[f]	0.94(d, *J*=6.4 Hz), 0.95(d, *J*=6.2 Hz), 1.29(d, *J*=6.4 Hz), 1.45(m), 1.82(m), 3.77(s), 4.45(br t, J=7.2 Hz), 5.10(sept, *J*=6.3Hz), 5.77(t, *J*=1.2 Hz), 6.18(d, *J*=0.7 Hz)	——	——	——
i-Bu	*t*-Bu	Me	**1h**	86	0.95(m), 1.51(s), 1.56(m), 3.78(s), 5.49(m),5.73(s), 6.20(s)	21.7, 23.1, 24.8, 28.0, 44.0, 54.6, 74.5, 81.2, 123.5, 142.2, 155.0, 164.2	1753, 1720, 1631, 792	216 (M^+ -isobutene)
			**5**[c]	71	0.98(m), 1.31(t, *J*=7 Hz, 1.82(m), 4.24(q, *J*=7 Hz), 5.70(m), 6.15(t, *J*=1.1 Hz), 6.22(d, *J*=1.1 Hz), 7.20-7.37(m)	14.2, 21.5, 23.0, 24.8, 43.8, 64.6, 72.9, 127.9, 146.0, [122.3, 127.2, 129.7, 149.5 Ar] 154.2	1820, 1749, 1586, 784	249 (M^+ -OPh)
			**6**	30[g]	0.94(d, *J*=6.2 Hz), 1.69(m), 3.03(br s) 3.79(s), 5.22(s), 5.33(m), 5.46(s)	21.8, 23.1, 24.7, 34.9, 38.6 43.1, 54.8, 76.9, 115.4, 144.1, 155.3, 169.4	1746, 1648 1630, 793	244 (M^+ +1)

a) Isolated yield of carbonate formation from allylic alcohols **3** and **4**, respectively.

b) Dimethyl 1,4-(4-vinyl-1-hexene)dicarboxylate was formed significantly (see ref. 19).

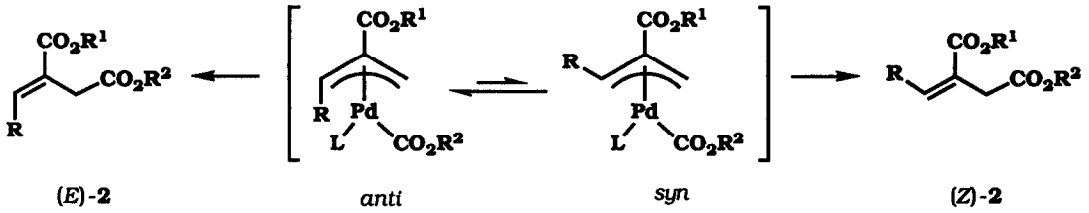
c) Ethyl chloroformate was used.

d) Ref. 4 and Deguchi, R. MC Thesis, Tokyo Institute of Technology (1985).

e) Recovery of **3e** (26%) was taken into account.

f) Recovery of **3g** (43%) was taken into account.

g) Precursor was 3-(methoxycarbonyloxy)-2-(*N*,*N*-dimethylaminomethyl)-5-methyl-*N*,*N*-dimethylhexanamide (**C** in Scheme 1).

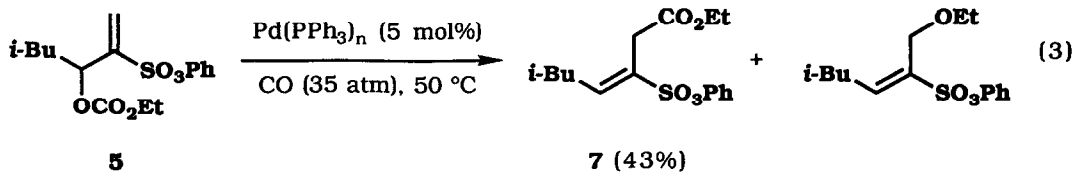


Scheme 2

disubstituted π-allylpalladium complexes in the *anti/syn* equilibrium are key intermediates that undergo carbonylation as depicted in Scheme 2. This is not necessarily the case, as is seen in Table II, since the substantial difference in steric bulk of R and R^1 was rather leveled to the uniform selectivity during a course of the reaction. Related but a little positive steric effects were observed in the Pd(0)-catalyzed carbonylation of 1-alkyl-2-trialkylsilyl-2-propenyl carbonates.[11] It is worth mentioning that, while an old procedure[12] which consists of a condensation of a nitroalkane with a dialkyl fumarate in the presence of diethylamine affords the corresponding dialkyl alkylidenesuccinate with a little higher *E* selectivity (95 : 5), the present catalytic carbonylation provides a sole product **2** which accommodates two different ester groups at will (Entries 3,5,8, and 9).

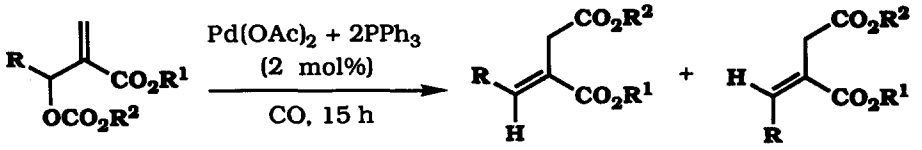
In order to examine the steric effect imposed by the other EWG than an ester group on the stereochemical outcome of the carbonylation products, we have carried out the Pd(0)-catalyzed carbonylation of phenyl 3-(ethoxycarbonyloxy)-5-methyl-1-hexene-2-sulfonate (**5**) and 3-(methoxycarbonyloxy)-5-methyl-2-methylene-*N,N*-dimethylhexanamide (**6**), respectively.

The carbonylation of **5** was not effectively catalyzed by the foregoing $Pd(OAc)_2$ + 2 PPh_3 but by $1/2Pd_2(dba)_3{\cdot}CHCl_3$ (dba = dibenzylideneacetone) + 2 PPh_3 (5 mol%) under a little forcing conditions [CO (35 atm), 50 °C for 36 h], giving ethyl (*E*)-6-methyl-3-phenoxysulfonyl-3-heptenoate (**7**)[13] (43% yield) and phenyl (*E*)-1-ethoxy-5-methyl-2-hexene-2-sulfonate [13] (7% yield), respectively (eq. 3). Thus, a complete *E* stereoregulation for the Pd(0)-catalyzed carbonylation *via* a π-allylpalladium intermediate is first realized by



5 **7** (43%)

Table II. Decarbonylative carbonylation of **1** giving alkylidenesuccinates **2**



1 (*E*)-**2** (*Z*)-**2**

Entry	Substrate				Conditions		2, Yield(%)[a]	2, *E*/*Z*[b]
		R	R^1	R^2	Temp (°C)	CO (atm)		
1	**1a**	Me	Me	Me	50	20	28[c]	93 : 7
2	**1b**	Me	Et	Et	100	50	55	91 : 9
3	**1c**	Me	*t*-Bu	Me	50	30	37[c]	92 : 8
4		Me	*t*-Bu	Me	100	50	55	90 : 10
5	**1d**	Et	*t*-Bu	Me	50	20	51	91 : 9
6	**1e**	*i*-Pr	Me	Me	50	20	67	93 : 7
7	**1f**	*i*-Bu	Me	Me	50	25	82	92 : 8
8	**1g**	*i*-Bu	*i*-Pr	Me	50	20	70	91 : 9
9	**1h**	*i*-Bu	*t*-Bu	Me	50	20	72	90 : 10

a) Isolated, combined yield.

b) Analyzed by a capillary column (HR-20M, 25 m × 0.24 mm) unless otherwise stated.

c) By-product 2-alkoxycarbonyl-1,3-butadiene formed as a dimer (see Ref. 19).

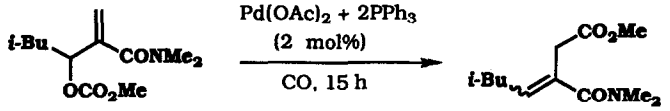
substituting such a bulky group as phenoxysulfonyl for any alkoxycarbonyl group in **1**. It should be noted that an ether formed as by-product in the carbonylation of **5** was also found to be an *E* isomer. This was not the case in the carbonylation of **1f**, where the by-product methyl ether always consisted of an *E*/*Z* isomeric mixture in a ratio 5 : 1.[4] These facts reinforce that a strong steric control in the *anti*-alkyl-π-allylpalladium intermediate can operate to give rise to the carbonylation product (*E*)-**7**.

Carbonylation of **6** was carried out under CO (30 atm) in otherwise the same manner as that of **1**, giving methyl 3-(3-methylbutylidene)-*N*,*N*-dimethylsuccinaminate (**8**) in satisfactory yield. However, the ratio of (*E*)-

and (Z)-**8** was found to be 30 : 70. Additional experiments were performed under various conditions in order to confirm the stereochemical outcome in giving **8**. Results are summarized in Table III. As is seen in Table III, the stereoselectivity did not alter appreciably by changing either CO pressure (Entries 1 and 3) or reaction temperature (Entry 4), being hard of preferring the *E* isomer.

Having found rather unexpected stereochemistry in this particular carbonylation of **6** in contrast to the high *E* selectivity for the carbonylation of **1**, we discuss briefly the reason why the reversed stereoselectivity was observed.

Table III. Decarboxylative Carbonylation of **6**



6 **8**

Entry	Temp (°C)	CO (atm)	**8**, Yield (%)[a]	**8**, *E*/*Z*[b]
1	50	10	75	41 : 59
2	50	30	75	30 : 70
3	50	50	62	37 : 63
4	100	30	79	43 : 57

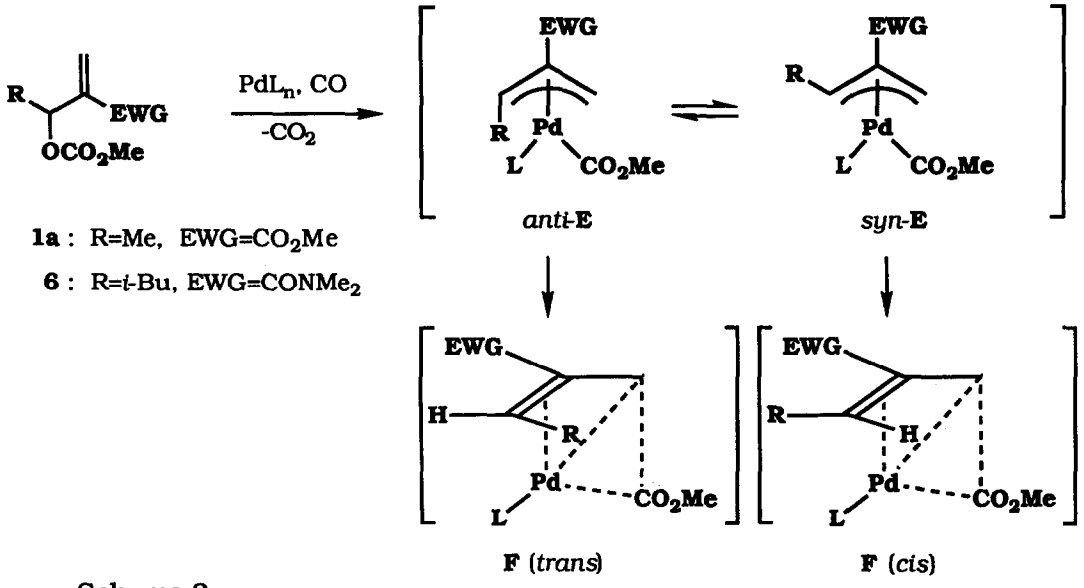
a) Isolated combined yield of the *E*/*Z* mixture.

b) Analyzed by a capillary column (HR-20M, 25 m × 0.24 mm).

c) *Examination of the reversed stereoselectivity for (E)-2a and (Z)-8 in the Pd(0)-catalyzed carbonylation of 1a and 6.*

It is premised that, under a CO pressure, a Pd(0) complex undergoes oxidative addition to the allylic carbonate with concomitant decarboxylation to form the π-allylpalladium alkoxide which, in turn, gives the corresponding alkoxycarbonyl complex **E**[14] essentially in *anti*/*syn* equilibrium as depicted in Scheme 3.

The recent mechanistic insight into the palladium complex-catalyzed reactions which involve the π-allylpalladium intermediate suggests that the reductive elimination will take place at mutual *cis* positions directly from the π-allyl ligand rather than the prior formation of the σ-allylpalladium moiety.[16] According to this view, the transient structures **F** (*trans* and *cis*) may apply for the transition states of the present reductive elimination starting from *anti*-**E** and *syn*-**E**, respectively. Namely, the stereoselectivity imposed by the carbonylation products must reflect the composition of these transient structures **F**, rather than that of π-allylpalladium intermediates **E** (the Curtin-Hammett principle).[11] Furthermore, the transient structures **F** are rather akin to



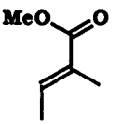
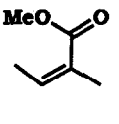
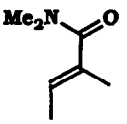
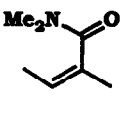
1a : R=Me, EWG=CO_2Me

6 : R=*t*-Bu, EWG=$CONMe_2$

Scheme 3

those of the σ-allylpalladium holding an olefinic part in coordination with the palladium center. For the first approximation, consequently, one may assume that there is no significant difference in a spacial interaction of the R group with the palladium center between **F**(*trans*) and **F**(*cis*) under otherwise equal situations. Since we have still no reliable parameters of bondings which involve the palladium moieties, it appears reasonable to examine the relative stability between geometrical differences in only the olefinic moieties extracted from the transient structures **F**(*trans*) and **F**(*cis*). On the basis of these premises, two compounds, methyl 2-methyl-2-butenoate (**9**) and *N,N*-dimethyl-2-methyl-2-butenamide (**10**), were adopted as the reliable models for transient structures **F** to simulate the observed stereoselectivities for the present carbonylation products **2a** and **8**, respectively. Thus, MM2 calculations of **9** and **10** for both *E* and *Z* isomers were carried out using Chem3DPlus program.[17] Optimization with respect to the RMS gradient less than 0.02 was completed by taking advantage of various dihedral angles which bear between a carbonyl group and an olefin plane. Two parameters generated from the most stable conformers of respective (*E*)/(*Z*)-**9** and -**10** are the dihedral angles (θ) and the total energy differences (ΔE) between these geometrical isomers. The results are given in Table IV. Significant features from Table IV may be three-fold: Firstly, while the dihedral angles of **9** indicate almost adequate coplanarity in both *E* and *Z* isomers, those of **10** are found to deviate remarkably from coplanar conformation. The extent of this deviation is larger in the (*Z*)-**10** than in the *E* isomer. Secondly, the difference in total steric energy, though it must be qualitative in nature, between (*E*)-**9** and (*Z*)-**9** is much advantageous for the former, whereas that of **10** is found to be inverted, the *Z* isomer being more stable than the *E* isomer. The fact that the steric bulk of *N,N*-

Table IV. Dihedral angles (θ) and total steric energy differences (ΔE) in the most stable conformers of **9** and **10**[a)]

	 (*E*)-**9**	 (*Z*)-**9**	 (*E*)-**10**	 (*Z*)-**10**
θ (deg)[b)]	180	176	-124	99
ΔE (kcal/mol)[c)]	-1.62[d)]			+1.02[e)]

a) Calculation using Chem3DPlus program.

b) Coplanarity taken as ±180 °.

c) Total steric energy difference, (*E*) - (*Z*).

d) (*E*)-**9** more stable than (*Z*)-**9**.

e) (*Z*)-**10** more stable than (*E*)-**10**.

dimethylamide group strongly prevents its coplanarity with the olefin moiety may explain these rather unusual results. The existing allylic strain between two methyl groups in mutual *cis* position ((*E*)-**9**) must be smaller than the steric repulsion between the methyl and the methoxycarbonyl group ((*Z*)-**9**). However, this is not the case for amide **10**. Since the amide group in **10** deviates from coplanar conformation by 56-81°, the allylic strain of two methyl groups in (*E*)-**10** emerges out of the other repulsive interactions. Finally, the foregoing arguments may apply to the transient structures **F** (Scheme 3), where **F** (*trans*, EWG = CO_2Me) is preferred over **F** (*cis*) to give the carbonylation product **2a** with 93% *E* selectivity. On the other hand, the carbonylation product **8** with 70% *Z* selectivity would be the direct consequence that **F** (*cis*, EWG = $CONMe_2$) is responsible for proceeding the transition state easier than **F** (*trans*).

In conclusion, we have carried out the novel Pd(0)-catalyzed carbonylation of 3-(methoxycarbonyloxy)-2-methylenealkanoate (**1**) and analogues which contain an EWG [SO_3Ph (**5**) or $CONMe_2$ (**6**)] other than an ester group in **1** and found that the stereochemical outcome of the carbonylation products differs remarkably each other. Particularly, the results of striking difference in stereoselectivities in the catalytic carbonylations of **1a** and **6** are explained in terms of the plausible MM2 simulation of the model compounds, **9** and **10**, which were extracted from the transient structures **F** presumed as the transition states of the present reaction.

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Experimental Section

General

Infrared spectra were recorded on a JASCO IR-700 spectrometer (neat). Nuclear magnetic resonance spectra were recorded on a JEOL JNM-FX-90Q FT NMR spectrometer (^{1}H, 90 MHz; ^{13}C, 22.5 MHz) in $CDCl_3$ using tetramethylsilane as a standard. GC-MS spectra were recorded on a JEOL JMS-AX500 mass spectrometer. Gas chromatography (GLC) analyses were performed on a Shimadzu Model GC-4C chromatograph. Capillary GLC analyses were performed on a Shimadzu Model GC-6A chromatograph. Peak areas were calculated on Shimadzu Model C-R3A chromatopac an automatic integrator. HPLC separations were performed on a Nihon Seimitsu Kagaku apparatus.

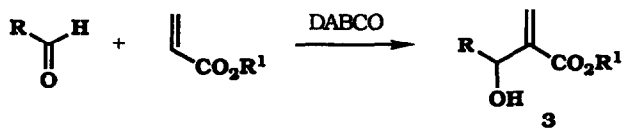
Materials

Allylic alcohols (**3**) were prepared according to the literature methods (the Baylis-Hillman reaction). In Table V are listed **3d** and **3h** newly prepared along with **3a-c** and **3e-g** prepared previously by others and by us. Preparation of phenyl 3-hydroxy-5-methyl-1-hexene-2-sulfonate (**4**) : A mixture of 3-methylbutanal (14 mL, 0.15 mmol), phenyl ethylenesulfonate (8 g, 43.4 mmol) and DABCO (0.5 g, 4.5 mmol) in benzene (80 mL) was stirred at r.t. for 3 h. The reaction mixture was washed with dil. HCl and brine, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane-CH_2Cl_2 4 : 1) to give **4** (10.3 g, 87%). ^{1}H NMR ($CDCl_3$, TMS) d 0.98(d, J=6.4 Hz), 1.67(m), 2.37(br d), 4.72(m), 6.13(s), 6.18(s), 7.25(m); ^{13}C NMR δ 21.5, 23.4, 24.7, 45.2, 67.8, [122.2, 127.2, 129.8, 149.4(Ar)], 127.3, 148.9; IR (cm^{-1}) 3530, 1586, 784.

(a) Preparation of 1, 5, and 6

(i) Preparation of alkyl 3-(methoxycarbonyloxy)-2-methylenealkanoate (**1**). A typical procedure for the preparation of **1b** is as follows: To a solution of **3b** (given in Table V) (14.4 g, 0.10 mol) in benzene (80 mL) were added ethyl chloroformate (14 mL, 0.15 mol), pyridine (8 mL, 0.1 mol), and 4-dimethylaminopyridine (DMAP; 1.22 g, 10 mmol) under cooling with an ice-bath. After being stirred at r.t. for 3 h, the reaction mixture was worked up as usual. The concentrated material was purified by column chromatography (silica gel, hexane-ether 4 : 1) to give **1b** (19.8 g, 92%). Spectral data of **1** are given in Table I. Analytical data are given below:

Table V. Preparation of 3-hydroxy-2-methylenealkanoate (3)



3

	R	R^1	Time(day)	Yield(%)	^{1}H NMR ($CDCl_3$, TMS) δ	Ref.
3a	Me	Me	7	95	1.39(d, *J*=6.4 Hz), 2.73(br d), 3.79(s), 4.6(m), 5.83(t, *J*=1.1 Hz), 6.22(t, *J*=0.7 Hz)	7)
3b	Me	Et	8	77	1.32(t, *J*=6.4 Hz), 1.38(d, *J*=6.6 Hz), 3.04(br d) 4.24(q, *J*=7 Hz), 4.63(m), 5.83(s), 6.21(s)	18)
3c	Me	*t*-Bu	15	63	1.38(d, *J*=6.6 Hz), 1.52(s), 2.65(br d), 4.57(br q), 5.72(s), 6.11(s)	19)
3d	Et	*t*-Bu	12	62	0.95(t, *J*=7 Hz), 1.51(s), 1.63(dq, *J*=7 Hz), 2.78(br d), 4.21(br q), 5.68(s), 6.12(s)	this work
3e	*i*-Pr	Me	7	51		4)
3f	*i*-Bu	Me	7	52		4)
3g	*i*-Bu	*i*-Pr	7	62		4)
3h	*i*-Bu	*t*-Bu	19	95	0.94(d, *J*=6.6 Hz), 1.48(m), 1.51(s), 2.58(br), 4.37(m), 5.70(s), 6.10(s)	this work

Calcd for $C_{10}H_{16}O_5$ (**1b**) C, 55.55; H, 7.46%. Found C, 54.00; H, 7.51%. $C_{11}H_{18}O_5$ (**1c**) C, 57.38; H, 7.88%. Found C, 57.76; H, 8.07%. $C_{12}H_{20}O_5$ (**1d**) C, 59.00; H, 8.25%. Found C, 58.56; H, 8.40%. $C_{14}H_{23}O_5$ (**1h**) C, 61.74; H, 8.25%. Found C, 61.84; H, 9.18%.

(ii) Preparation of phenyl 3-(ethoxycarbonyloxy)-5-methyl-1-hexene-2-sulfonate (**5**). From phenyl 3-hydroxy-5-methyl-1-hexene-2-sulfonate (**4**) was prepared **5** (Table I) as follows: To a suspension of NaH (55% in mineral oil 0.5 g, 11.5 mmol) in ether (20 mL) were added **4** (1 g, 3.7 mmol), ethyl chloroformate (2.8 mL, 30 mmol), and dicyclohexano-18-crown-6 (0.15 g, 0.36 mmol) with stirring. The mixture was heated at reflux for two weeks. By usual work-up and purification was obtained **5** in 71% yield. Anal. Calcd for $C_{16}H_{23}O_6S$ C, 56.13; H, 6.48; S, 9.36%. Found C, 56.19; H, 6.53; S, 9.23%.

(iii) Preparation of 3-(methoxycarbonyloxy)-5-methyl-2-methylene-*N,N*-dimethylhexanamide (**6**)

To a solution of 2-(*N,N*-dimethylaminomethyl)-3-hydroxy-5-methyl-*N,N*-dimethylhexanamide (**A**) (10 g,

43.4 mmol), which was prepared by the addition of an enolate of 3-(*N*,*N*-dimethylamino)-*N*,*N*-dimethylpropanamide to 3-methylbutanal,[9] in CH_2Cl_2 (50 mL) was added methyl chloroformate (5 mL, 64.7 mmol) under cooling with an ice-water bath. After being stirred at r.t. for 5 h, the reaction mixture was extracted with cold diluted HCl. The extract was washed with CH_2Cl_2, neutralized with NaOH, and the organic materials was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 3-(methoxycarbonyloxy)-5-methyl-2-(*N*,*N*-dimethylaminomethyl)-*N*,*N*-dimethylhexanamide (C) (12.4 g, 99.5%).

To a solution of compound C (12.4 g, 43.2 mmol) in CH_2Cl_2 (200 mL) was added *m*-chloroperoxybenzoic acid (purity 80%, 10 g, 46.4 mmol) under cooling in an ice-water bath. After being stirred at r.t. for 15 h, the reaction mixture was eluted through a column containing basic alumina (Merck, aluminium oxide 60 active, basic) with CH_2Cl_2 (200 mL) to give 3-(methoxycarbonyloxy)-5-methyl-2-methylene-*N*,*N*-dimethylhexanamide (**6**) (3 g, 30%). Anal. Calcd for $C_{12}H_{21}NO_4$ C, 59.24; H, 8.70; N, 5.76%. Found C, 59.52; H, 8.98; N, 5.75%. Spectral data for **5** and **6** are given in Table I.

(b) General procedure for Pd(0)-catalyzed carbonylation of 1, 5 and 6

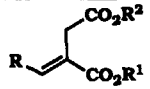
To a mixture of allylic carbonate **1** (1 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), and PPh_3 (10.5 mg, 0.04 mmol), placed in a glass tube fitted to a 50 mL micro-autoclave, was introduced CO (20-50 atm) after careful removal of air. The mixture was heated at 50-100 °C for 15 h with magnetic stirring. The resulting reaction mixture was passed through a short Florisil column by elution with ether. The etheral filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexane-ether 10 : 1) to give the corresponding carbonylation products. The ratio of (*E*)-/(*Z*)-alkylidenesuccinate (**2**) was determined by capillary GLC (HR-20M, 25 m × 0.24 mm, N_2). Carbonylation of **6** was carried out in exactly the same manner as above and product **8** was analyzed by capillary GLC to determine the *E*/*Z* ratio and isolated as usual and by preparative HPLC.

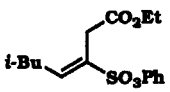
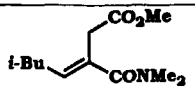
A mixture of **5** (342 mg, 1.0 mmol) and $Pd(PPh_3)_n$ (5 mol%), prepared *in situ* from $Pd_2(dba)_3$•$CHCl_3$ (26 mg, 0.025 mmol) and PPh_3 (26 mg, 0.1 mmol) was heated at 50 °C for 36 h under a CO pressure (35 atm). Usual work-up and column chromatography afforded **7** (140 mg, 43%) and phenyl (*E*)-1-ethoxy-5-methyl-2-hexene-2-sulfonate (21 mg, 7%). HPLC analysis revealed that the product **7** and the by-product were geometrically homogeneous. The results are summarized in Tables II and III, respectively. All spectral and analytical data are given in Table VI.

(c) MM2 calculations on 9 and 10

Calculations were preformed using Chem3DPlus (ver. 2.0.1) program.[15] General parameters were input to calculate structures of methyl 2-methyl-2-butenoate (**9**) and *N*,*N*-dimethyl-2-methyl-2-butenamide (**10**), for both *E* and *Z* geometrical isomers, respectively. Both *s-cis* and *s-trans* conformers were also taken into account as the initial structures. Final energies and all coordinates for optimized geometries are given below (see also Table IV).

Table VI. Special and analytical data for **2**, **7**, and **8**



R	R^1	R^2	Entry	^{1}H NMR($CDCl_3$,TMS),[a] δ	^{13}C NMR,[a] δ	Capillary GLC,[b] t_R (min)	Anal. (Calcd) C,	H,	Others
Me	Me	Me	**2a** (*E*)	1.84(d, *J*=7.3 Hz), 3.37(s), 3.69(s), 3.75(s). 7.08(q, *J*=7.3 Hz)	14.1, 31.5, 51.5(×2), 126.3, 140.3 166.9, 170.8	4.8 (*E*)			
			2a (*Z*)	2.09(d, *J*=7.3 Hz), 3.27(s), 3.72(s), 3.73(s), 6.22(q, *J*=7.3 Hz)		3.8 (*Z*)			
Me	Et	Et	**2b**	1.25(t, *J*=7 Hz), 1.28(t, *J*=7 Hz), 1.84(d, *J*=7.3 Hz), 3.35(s), 4.15(q, *J*=7.3 Hz), 4.20(q, *J*=7 Hz), 7.06(q, *J*=7.3 Hz)(*E*); 6.13(q, *J*=7 Hz)(*Z*)	14.1, 14.5(×2), 32.1, 60.7(×2), 126.9, 140.1, 166.8, 170.7	6.0 (*E*) 4.9 (*Z*)	60.11 (59.66)	8.32 (8.05)	
Me	*t*-Bu	Me	**2c**	1.47(s), 1.81(d, *J*=7.3 Hz), 3.32(s), 3.69(s), 6.96(q, *J*=7.3 Hz)(*E*); 6.14(q, *J*=7 Hz)(*Z*)	14.4, 28.1, 32.0, 51.7, 80.5, 128.1, 139.0, 166.0, 171.3	4.7 (*E*) 3.9 (*Z*)	61.75 (61.66)	8.64 (8.47)	
Et	*t*-Bu	Me	**2d**	1.06(t, *J*=7.5 Hz), 1.47(s), 2.18(d, *J*=7.5 Hz), 3.29(s), 3.67(s), 6.85(t, *J*=7.5 Hz)(*E*); 5.97(t, *J*=7 Hz)(*Z*)	12.8, 22.0, 27.9, 32.1, 51.6, 80.4, 126.5, 145.5, 166.0, 171.3	5.5 (*E*) 4.3 (*Z*)	62.56 (63.14)	8.97 (8.83)	
i-Bu	*t*-Bu	Me	**2h**	0.93(d, *J*=6.4 Hz), 1.47(s), 1.56(m), 3.30(s), 3.68(s), 6.89(t, *J*=7.5 Hz)(*E*); 5.98(t, *J*=7 Hz)(*Z*)	22.4(×2), 27.8, 28.0, 32.5, 37.8, 51.7 80.6, 127.5, 143.3, 168.9, 171.5	8.7 (*E*) 7.6 (*Z*)	62.88 (65.60)	9.13 (9.44)	
			**7** (*E*)	0.86(t, *J*=6.4 Hz), 1.27(t, *J*=7 Hz), 1.73(m), 2.12(dd, *J*=6.6, 7.3 Hz), 3.55(s), 4.20(q, *J*=7 Hz), 6.8(t, *J*=7.3 Hz), 7.3(m)	14.1, 22.3(×2), 28.0, 32.5, 37.9, 61.5 [122.2, 127.0, 129.7, 149.7(Ar)], 127.0, 144.8, 168.3		59.62 (58.88)	6.65 (6.79)	S 9.68 (9.82)
			**8** (*E*)	0.93(d, *J*=6.4 Hz), 1.65(m), 2.03(dd, *J*=6.2, 7.3 Hz), 3.06(br s), 3.44(s), 3.66(s), 5.75(t, *J*=7.3 Hz)	22.4(×2), 28.4, 33.7, 37.0, 38.0(br), 51.7, 129.0, 134.0, 171.5	8.2[c]	62.75 (63.41)	9.50 (9.31)	N 5.88 (6.16)
			8 (*Z*)	0.90(d, *J*=6.4 Hz), 1.61(m), 1.89(dd, *J*=6.0, 7.3 Hz), 3.01(s), 3.07(s), 3.34(s), 3.67(s), 5.55(t, *J*=7.3 Hz)	22.4(×2), 28.2, 34.3, 37.9, 38.4, 40.3, 51.7, 129.1, 132.0, 170.2, 171.5	6.7[c]			

a) Diagnostic olefin protons or allylic carbons underlined. b) HR-20M (25 m × 0.24 mm) at 150 °C unless otherwise stated. c) Retention time (t_R) at 170 °C.

Compound Energies	(*E*)-**9**	(*Z*)-**9**	(*E*)-**10**	(*Z*)-**10**
Stretch	0.6299	0.5825	0.3687	0.3065
Bend	3.1462	3.5175	1.7688	1.4401
Stretch-Bend	0.0699	0.0747	-0.0199	-0.0027
Torsion	-4.7048	-3.1672	2.1079	2.4604
Non-1,4 VDW	0.9140	0.6904	-0.3723	-1.0685
1,4 VDW	4.9077	4.8823	4.0916	3.7240
Dipole/Dipole	1.2706	1.2694	-9.2325	-9.1654
Total (kcal/mol)	6.2335	7.8500	-1.2877	-2.3056
Dihedral angle (θ)	179.68°	175.86°	-123.85°	98.82°
RMS Gradient (kcal/Å-mol)	0.01	0.01	0.02	0.01

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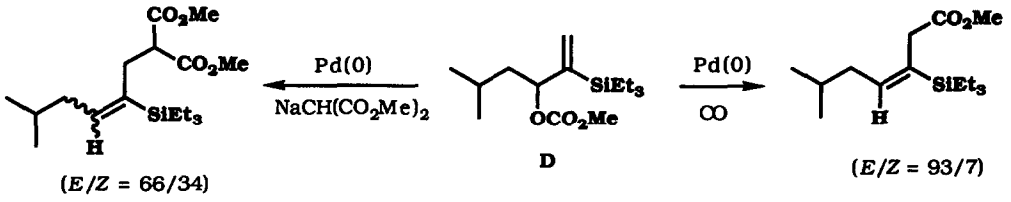
11) Wang, S.-Z.; Yamamoto, K. *Chem. Lett.* **1991**, 1993 and unpublished data: While Pd(0)-catalyzed carbonylation of 1-isobutyl-2-triethylsilyl-2-propenyl methyl carbonate (**D**) gave methyl (*E*)-3-triethylsilyl-6-methyl-3-heptenoate along with the *Z* isomer in a ratio 93 : 7, the Pd(0)-catalyzed alkylation of **D** with dimethyl sodiomalonate afforded dimethyl (*E*)- and (*Z*)-2-triethylsilyl-5-methyl-2-hexenylmalonate in a ratio 66 : 34. The striking difference in *E*/*Z* selectivities for these two reactions must reflect the substantially different transition states of respective reaction.



(*E*/*Z* = 66/34) **D** (*E*/*Z* = 93/7)

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13) Diagnostic chemical shifts of allylic carbons always appeared at upper field for an *E* isomer compared with a *Z* isomer in reference to **8** (see Table VI).

14) There are two possible paths for carbon monoxide insertion:[1)] One is the insertion of CO into the π-allylpalladium bond giving a 3-alkenoylpalladium alkoxide. Another one is the insertion into the palladium-alkoxide bond to give an alkoxycarbonyl complex. It is thus presumed that the latter is more probable on the basis of related carbonylation reactions.[15)]

15) Although there is no report which deals with the mechanistic detalils on the Pd(0)-catalyzed carbonylation of allylic substrates, those of CO insertion into the methyl(alkoxo)palladium(II) may be of significance: Kim, Y.-J.; Osakada, K.; Sugita, K.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1988**, *7*, 2182.

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