Isomerization of (π-Allyl)palladium Complexes via Nucleophilic Displacement by Palladium(0). A Common Mechanism in Palladium(0)-Catalyzed Allylic Substitution

Kenneth L. Granberg and Jan-E. Bäckvall*

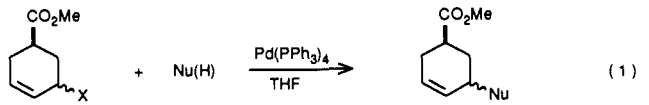
Contribution from the Department of Organic Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala, Sweden. *Received May 20, 1991*

Abstract: Treatment of (π-allyl)palladium complexes such as **6** and **9** with $Pd(PPh_3)_4$ leads to rapid isomerization at −15 °C in tetrahydrofuran and other solvents. At 0 °C and in the presence of more than 2 equiv of triphenylphosphine per palladium, the phosphine attacks the π-allyl group to give allylic phosphonium salts **7** with concomitant formation of a palladium(0)–phosphine complex, and isomerization of **6** is observed. Attack by PPh_3 on **6** was shown to be stereospecific and to proceed with inversion. Studies of the Pd(0)-catalyzed substitution of **1c** (X = OAc) with several different nucleophiles support the hypothesis that Pd(0) acts as a nucleophile on (π-allyl)palladium complexes, in a reaction that leads to loss of stereospecificity in these systems.

Introduction

Pd(0)-catalyzed nucleophilic substitution of allylic compounds has been established as an important synthetic method for C–C, C–N, and C–O bond formation in inter-[1] and intramolecular[2] reactions. One of the reasons for its success is the facile reaction of allylic substrates having leaving groups such as carboxylates. Another important feature of the reaction is the high stereospecificity with which a number of nucleophiles are added. In many cases, however, loss of stereospecificity is observed.[3] Several mechanisms have been suggested to account for the loss of stereospecificity: (i) isomerization of starting material, (ii) syn addition of nucleophile, (iii) isomerization of product, and (iv) Pd(0)-catalyzed isomerization of the intermediate π-allyl complex.

We have recently shown that the leaving group has a dramatic effect on the stereospecificity of the Pd(0)-catalyzed conversion of **1** (**a**–**d**) to **2** (**a**, **b**), (eq 1).[4] Thus, the stereospecificity was



(1)

1a X = Cl
b X = O_2CCF_3
c X = O_2CCH_3
d X = O_2COCH_3

2a Nu = $CH(SO_2Ph)_2$
b Nu = NEt_2

shown to increase with the reactivity of the leaving group. One of our conclusions was that the major pathway for the formation of the anomalous substitution product (overall inversion) involves nucleophilic attack by free Pd(0) on the (π-allyl)palladium intermediate.[4] In order to obtain further evidence for this mechanism we have now studied the reactions of Pd(0) complexes with the (π-allyl)palladium intermediates involved in eq 1 and estimated the rate constants for this isomerization reaction.

The Pd(0)-catalyzed isomerization has been suggested by Tsuji[5a] and Bosnich et al.[5b] to operate in acyclic systems but has not received wide recognition, probably due to the complexity of the systems studied.[5c] The (π-allyl)palladium complexes studied in this paper are directly related to catalytic systems on which thorough mechanistic studies have already been made.[4,6]

Table I. Effects of Added PPh_3 and $Pd(PPh_3)_4$ on the Isomerization of **6**[a,b] and Dependence of Temperature on the Time to Reach Equilibrium (T_{eq})

entry	solvent	π-allyl complex	temp (°C)	phosphine, equiv	Pd(0)–phosphine complex, equiv	T_{eq} (min)
1	$CDCl_3$	*cis*-**6**	0	PPh_3, 2	$Pd(PPh_3)_4$, 0.5	<5
2	$CDCl_3$	*trans*-**6**	0	PPh_3, 2	$Pd(PPh_3)_4$, 0.5	<5
3	$CDCl_3$	*cis*-**6**	−14	PPh_3, 2	$Pd(PPh_3)_4$, 0.5	25
4	$CDCl_3$	*trans*-**6**	−13	PPh_3, 2	$Pd(PPh_3)_4$, 0.5	20
5	$CDCl_3$	*cis*-**6**	−14	–	$Pd(PPh_3)_4$, 1.0	<5
6	$CDCl_3$	*cis*-**6**	−15	PPh_3, 2	–	∞
7	$CDCl_3$	*cis*-**6**	2	PPh_3, 2	–	15
8	$CDCl_3$	*cis*-**6**	20	–	–	∞
9	THF	*cis*-**6**	20	–	–	∞
10	THF	*trans*-**6**	20	–	–	∞
11	THF	*cis*-**6**	20	PPh_3, 2	–	<5

[a] Compounds *cis*- and *trans*-**6** were obtained in situ from **4**. [b] See Table II for the concentration of added compounds.

Results

A. Preparation of (π-Allyl)palladium Complexes. The syntheses of *cis*- and *trans*-**3** from *trans*-**1a** were straightforward and highly stereospecific by use of known methods[7] with a few modifications.[8] Abstraction of the chloride in **3** with silver trifluoromethanesulfonate in methylene chloride gave the corresponding triflate complex **4**, which was isolated in 98% yield. The reaction of these complexes with PPh_3 was studied by ^1H and ^{31}P NMR spectroscopy, and some of the complexes observed are shown in Scheme I.

B. Isomerization of π-Allyl Intermediates Catalyzed by Palladium(0). To test our hypothesis that Pd(0) displacement of palladium in (π-allyl)palladium intermediates is a common pathway for the isomerization in palladium-catalyzed allylic substitutions, we studied both stoichiometric and catalytic reactions.

1. Reaction of Isolated (π-Allyl)palladium Complexes with Pd(0). Addition of 0.5 equiv of $Pd(PPh_3)_4$ and 2 equiv of PPh_3 to *cis*- or *trans*-**6** in $CDCl_3$ at 0 °C resulted in a very fast isomerization (Table I, entries 1 and 2) to give an equilibrium mixture of *cis*-**6** (45%) and *trans*-**6** (55%) (K_{eq} = 1.22). Even at −14 °C

(1) (a) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer Verlag: Berlin, 1980. (b) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (c) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon Press: Oxford, 1982; Vol. 8, p 799.

(2) (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1173. (b) Bäckvall, J. E. *New J. Chem.* **1990**, *14*, 447.

(3) (a) Trost, B. M.; Keinan, E. *J. Am. Chem. Soc.* **1978**, *100*, 7779. (b) Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, 2301. (c) Keinan, E.; Sahai, M.; Roth, Z. *J. Org. Chem.* **1985**, *50*, 3558. (d) Oppolzer, W.; Gaudin, J. M.; Birkinshaw, T. N. *Tetrahedron Lett.* **1988**, *29*, 4705. (e) Bäckvall, J. E.; Vågberg, J. O.; Granberg, K. L. *Tetrahedron Lett.* **1989**, *30*, 617. (f) Stary, I.; Kočovsky, P. *J. Am. Chem. Soc.* **1989**, *111*, 4981.

(4) Bäckvall, J. E.; Granberg, K. L.; Heumann, A. *Isr. J. Chem.* **1991**, *31*, 17.

(5) (a) Takahashi, T.; Jinbo, Y.; Kitamura, K.; Tsuji, J. *Tetrahedron Lett.* **1984**, *25*, 5921. (b) MacKenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046. (c) The first suggestion in print for isomerization due to Pd–Pd exchange was given by Collman and Hegedus: Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: CA, 1980; p 692.

(6) (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

(7) (a) Kurosawa, H.; Ogoshi, S.; Kawasaki, Y.; Murai, S.; Miyoshi, M.; Ikeda, I. *J. Am. Chem. Soc.* **1990**, *112*, 2813. (b) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.

(8) In the synthesis of *cis*-**3** we used $Pd(dba)_2$ instead of $Pd_2(dba)_3$ since the former is easier to synthesize and gives the same stereochemical result in high yields. It is furthermore essential to use $Pd_2(dba)_3C_6H_6$ and not $Pd_2(dba)_3CHCl_3$ in benzene for the synthesis of *trans*-**3** since the latter gave only 80% syn addition while the former gave 95% syn on a 1-mmol scale.

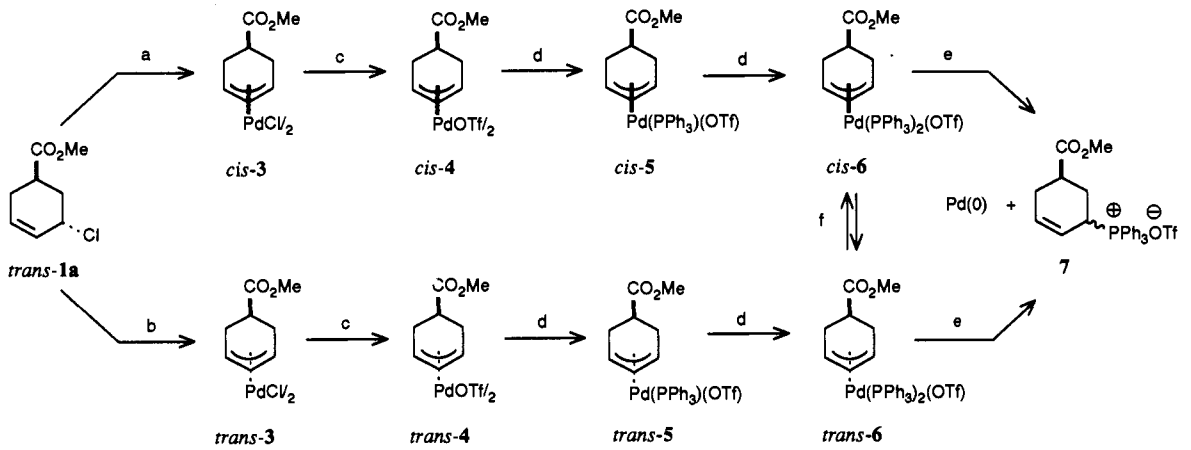
0002-7863/92/1514-6858$03.00/0 © 1992 American Chemical Society

Table II. Calculated Rate Constants[a] for the $Pd(PPh_3)_4$-Catalyzed Isomerization of **6**[b]

isomer of **6**	temp (°C)	substrate (10^{-3} M)	PPh_3 (10^{-3} M)	$Pd(PPh_3)_4$ (10^{-3} M)	$k_1^{obsd} \times 10^3$ (M^{-1} s^{-1})[c]	$k_{-1}^{obsd} \times 10^3$ (M^{-1} s^{-1})[c]
cis	−13.6	15.2	90.4	15.2	105 ± 7	86 ± 7
trans	−14.3	16.8	134	16.8	95 ± 7	78 ± 7

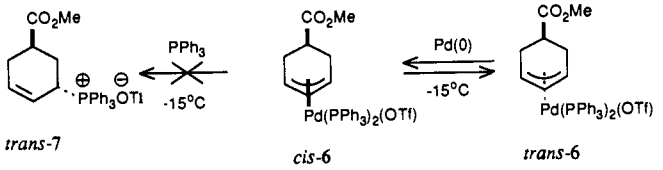
[a] Second-order reactions were assumed. [b] In $CDCl_3$; **6**:$Pd(PPh_3)_4$:PPh_3, 1:1:8. [c] See footnote 9.

Scheme I[a]

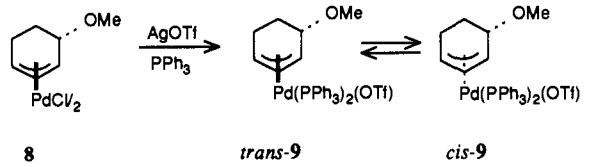


[a] Tf = SO_2CF_3. Reagents and conditions: (a) $Pd(dba)_2$, DMSO, 2 h, (95%); (b) $Pd_2(dba)_3C_6H_6$, C_6H_6, 22 h, (85%); (c) AgOTf, CH_2Cl_2, 0.5 h, (98%); (d) PPh_3 (1 equiv/Pd); (e) PPh_3; (f) $Pd(PPh_3)_4$.

Scheme II



Scheme III



this isomerization took only 25 min to reach equilibrium (Table I, entry 3). The isomerization of **6** was followed by ^1H and/or ^{31}P NMR spectroscopy at −14 °C (Table I, entries 3 and 4), which allowed the estimation of the rate constants of the isomerization (Table II, vide infra). Addition of only $Pd(PPh_3)_4$ at −14 °C led to an equilibrium in <5 min (Table I, entry 5), which is considerably faster than if both PPh_3 and $Pd(PPh_3)_4$ were added (Table I, entry 3). Apparently, PPh_3 decreases the formation of nucleophilic $Pd(PPh_3)_{4-n}$ where n = 1 or 2. A control experiment with addition of only PPh_3 to *cis*-**6** at −15 °C showed that no isomerization took place under these conditions (Table I, entry 6; Scheme II). However, at an elevated temperature (+2 °C), isomerization was observed when only phosphine was added (Table I, entry 7). The reason for the latter isomerization will be discussed below.

We also studied the isomerization of complex *trans*-**9** (Scheme III). Synthesis and isolation of the corresponding triflate complex of **8** by treatment with AgOTf was unsuccessful due to rapid decomposition. However, prior addition of phosphine to **8** followed by treatment with AgOTf and filtration gave the desired complex *trans*-**9** in situ, as shown by ^1H NMR spectroscopy. Addition of more than 2 equiv of triphenylphosphine in $CDCl_3$ rapidly (<5 min at 0 °C) led to a 1:2 mixture of *cis*-**9** and *trans*-**9** together with small amounts of side products.

2. Estimation of the Rate of Isomerization of 6. Rate constants for the Pd(0)-catalyzed isomerization of **6** in $CDCl_3$ are given in Table II. These rate constants were obtained by solving the simple expression (eq 3) for a second-order catalyzed equilibrium (eq 2) as shown below, followed by plotting $\ln|1 - (K_{eq} + 1)[cis\text{-}6]/[6]|$ versus time (K_{eq} = 1.22), the slope being equal to $-(k_1 + k_{-1})[Pd(PPh_3)_{4-n}]$. As expected, a linear relationship was ob-

$$cis\text{-}6 + Pd(PPh_3)_{4-n} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} trans\text{-}6 + Pd(PPh_3)_{4-n} \quad (2)$$

$$\frac{d[cis\text{-}6]}{dt} = [Pd(PPh_3)_{4-n}]\left(k_{-1}[trans\text{-}6] - k_1[cis\text{-}6]\right) \quad (3)$$

$$[6] = [cis\text{-}6] + [trans\text{-}6] \quad (4)$$

$$K_{eq} = k_1 / k_{-1} \quad (5)$$

$$\ln\left|1 - \frac{[cis\text{-}6]}{[6]}(1 + K_{eq})\right| = k't \quad (6)$$

$$k' = -(k_1 + k_{-1})[Pd(PPh_3)_{4-n}] \quad (7)$$

tained. The results from the isomerization starting from either *cis*-**6** or *trans*-**6** are given in Table II. From these data, average values of k_1^{obsd} = 0.10 M^{-1} s^{-1} and k_{-1}^{obsd} = 0.08 M^{-1} s^{-1} are obtained.[9] Solubility problems in THF prevented determination of the rate constants for the equilibration in that solvent at low temperatures, but we have concluded from competition experiments that isomerization was complete at least 10 times faster in THF than in $CDCl_3$ at −15 °C. These rate constants are considerably larger than the estimated rate constant for Pd(0)-catalyzed substitution of **1c**.[10] The reason why the Pd(0)-

(9) (a) The rate constants k_1^{obsd} and k_{-1}^{obsd} calculated in Table II were obtained by assuming that the active palladium(0) species was present in the same concentration as the amount of added $Pd(PPh_3)_4$. This is an oversimplification since the amount of active Pd(0) catalyst might be very small (especially if $Pd(PPh_3)_2$ is the active species).[9b] The true values k_1 and k_{-1} are given by the expression $k_1^{obsd} = k_1K_n$ and $k_{-1}^{obsd} = k_{-1}K_n$, where K_n is the equilibrium constant for $Pd(PPh_3)_4 \rightleftarrows Pd(PPh_3)_{4-n} + nPPh_3$. Thus the true rate constants must always be larger than those observed. (b) It is known that in solutions of $Pd(PPh_3)_4$ in THF the major species is $Pd(PPh_3)_3$ with small amounts of $Pd(PPh_3)_2$: Mann, B. E.; Musco, A. *J. Chem. Soc., Dalton Trans.* **1975**, 1673. Kuran, W.; Musco, A. *Inorg. Chim. Acta* **1975**, *12*, 187. Fauvarque, J. F.; Phlüger, F.; Troupel, M. *J. Organomet. Chem.* **1981**, *208*, 419. Amatore, C.; Phlüger, F. *Organometallics* **1990**, *9*, 2276. Amatore, C.; Azzabi, M.; Jutand, A. *J. Am. Chem. Soc.* **1991**, *113*, 8375.

Table III. Stereospecificity in Pd(0)-Catalyzed Allylic Substitution of *cis*- and *trans*-**1c**[a]

entry	substrate (concn 10^{-3} M)	catalyst (%)	nucleophile[b]	time (h)	conversn (%)	product[c] [cis]/[trans]	substrate[d] [cis]/[trans]
1	*cis*-**1c** (125)	$Pd(PPh_3)_4$ (5)	A	1	50	18.6	199
				12	100	18.2	
2	*cis*-**1c** (125)	$Pd(PPh_3)_4$ (24)	A	1	80	13.8	199
				5	100	11.2	
				12	100	11.3	
3	*cis*-**1c** (125)	$Pd(dppe)_2$ (5)	A	1	100	199	
4	*cis*-**1c** (432)	$Pd(PPh_3)_4$ (2)	A	0.5	37	24.6	166
				1.7	79	22.8	332
				5	100	18.6	
5	*cis*-**1c** (35)	$Pd(PPh_3)_4$ (25)	A	0.25	6	21.0	142
				0.5	15	26.5	166
				1.1	39	15.7	
				5	100	9.4	
6	*cis*-**1c** (125)	$Pd(dppe)_2$ (5)	B	19	76	40.7	199
7[e]	*cis*-**1c** (125)	$Pd(PPh_3)_4$ (5)	B	3.0	30	2.0	199
8[e]	*trans*-**1c** (125)	$Pd(PPh_3)_4$ (5)	B	4.0	54	0.35	199
9	*cis*-**1c** (125)	$Pd(dppe)_2$ (5)	C	0.17	33	49.0	57.8
				0.83	89	70.4	7.4
				1.67	100	26.0	
10[d]	*cis*-**1c** (125)	$Pd(PPh_3)_4$ (5)	C	3.0	36	2.0	2.6

[a] All reactions were run in THF at 50 °C under inert atmosphere. [b] A = $NaCH(CO_2Me)_2$; B = $NaCH(SO_2Ph)_2$; C = $HNEt_2$. [c] Determined by ^1H NMR spectroscopy or GC. [d] Reminaing substrate analyzed by ^1H NMR spectroscopy or GC. [e] Reference 4.

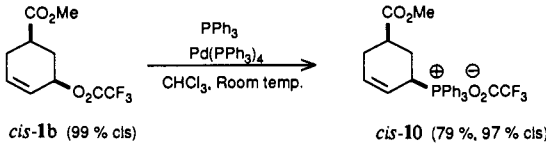
catalyzed reaction can still be stereospecific will be discussed below.

The effect of the solvent on the Pd(0)-catalyzed isomerization of *cis*- and *trans*-**6** was studied. The isomerization in solvents such as THF, chloroform, acetone, and acetonitrile was fast and of comparable rate whereas in benzene the isomerization was slower. The equilibrium constant K_{eq} between *cis*- and *trans*-**6** (eq 2) varied slightly between different solvents and increased with the polarity of the solvent (benzene, 1.17; chloroform, 1.20; THF, 1.22; acetonitrile, 1.42; dimethyl sulfoxide, 1.47; acetone, 1.53).

3. Effect of $[Pd(PPh_3)_4]$ on the Stereospecificity of the Pd(0)-Catalyzed Substitution of 1c. A method for observation of a Pd(0)-catalyzed isomerization of the intermediate π-allyls has been to study the effect of the concentration of the catalyst ($Pd(PPh_3)_4$) on the stereospecificity of a certain reaction, since the mechanism requires the rate of the isomerization step to be proportional to the concentration of the metal.[4,5a] Studies of the catalytic reactions shown in Table III showed that there is a definite dependence of the stereospecificity on the concentration of the catalyst,[5a] i.e., an increased amount of added catalyst resulted in an increased loss of stereospecificity (compare Table III, entry 1 versus 2 and 4 versus 5; in entries 4 and 5 the concentration of added catalyst was kept constant[11]). This confirms the observations made on isolated intermediates, which showed that the presence of free Pd(0) correlates with isomerization of the free π-allyl. Table III also demonstrates that isomerization of the starting material **1c** (X = OAc) is negligible in all cases where carbon nucleophiles are used (Table III, entries 1–8), in contrast to what has been suggested[3b,6] in cases where a stereorandomized product is obtained. Control experiments showed that no detectable isomerization due to enolization at the α-carbon to the carbomethoxy group of either starting material or product occurred under the reaction conditions.[4]

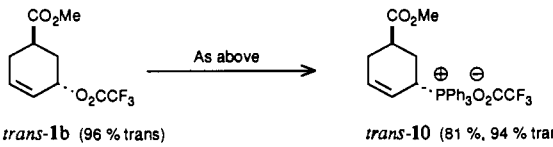
C. Nucleophilic Attack by PPh_3 on (π-Allyl)palladium Complexes. The addition of PPh_3 to *cis*-**6** at a temperature >0 °C resulted in an isomerization to *trans*-**6** and the formation of two new organic compounds. With an excess of PPh_3 and heating to 50 °C a complete conversion of the isomeric (π-allyl)palladium complexes (**6**) to allylic phosphonium salts **7**, cis and trans, was observed (Scheme I). Clearly, an attack by PPh_3 has taken place on the (π-allyl)palladium complex. During this process a Pd(0)–phosphine complex is released, which would account for the isomerization.

Attack by PPh_3 on (π-allyl)palladium complexes has been reported[12] previously, but the stereochemistry of the addition is unknown. One could argue that PPh_3, being a very good ligand for palladium, would add to the π-allyl ligand via cis migration as has been observed for nonstabilized carbon nucleophiles,[13] hydride,[14] and in some cases, carboxylates.[15] However, reaction of *cis*-**1b** and *trans*-**1b** with PPh_3 in the presence of $Pd(PPh_3)_4$ (eqs 8 and 9) proceeded with overall retention (98%). Since the



(8)

cis-**1b** (99 % cis) *cis*-**10** (79 %, 97 % cis)



(9)

trans-**1b** (96 % trans) *trans*-**10** (81 %, 94 % trans)

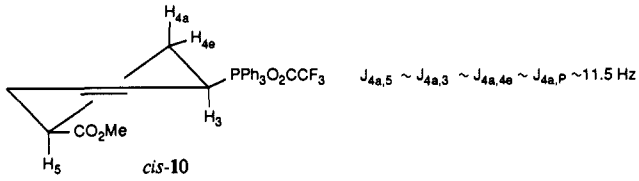
oxidative addition of $Pd(PPh_3)_4$ to give π-allyl intermediates is known to take place with inversion,[16] the stereochemistry of the products requires that PPh_3 has attacked the π-allyl intermediate trans.

The assignment of *cis*-**10** is based on its ^1H NMR spectrum. Four large coupling constants of ~11.5 Hz for H_{4a} indicate that both CO_2Me and $PPh_3O_2CCF_3$ occupy pseudoequatorial positions. The corresponding chlorophosphonium salt as the cis isomer[17] was obtained from *trans*-**1a** in the same manner as **8** from **1b**. This

(10) A direct comparison between the rate of the isomerization of *cis*- and *trans*-**6** and the rate of the catalytic reaction of **1c** cannot be made since the π-allyl complexes involved have different counterions (TfO^- and OAc^-, respectively). Attempts to study the isomerization of the corresponding π-allyl complex with acetate as the counterion failed because of competing formation of **1c**.

(11) One can argue that in order to obtain meaningful results the concentration of added $Pd(PPh_3)_4$ should be constant in all reactions under comparison since the degree of dissociation of the parent Pd(0) complex to unsaturated species will vary with the concentration of $Pd(PPh_3)_4$.

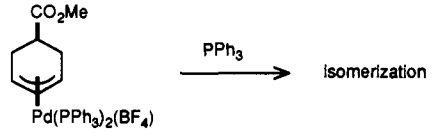
(12) (a) Powell, J.; Shaw, B. L. *J. Chem. Soc. A* **1968**, 774. (b) Tsukahara, Y.; Kinoshita, H.; Inomata, K. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3013.
(13) Matsushita, H.; Negishi, E. *J. Org. Chem.* **1982**, *47*, 4161.
(14) (a) Hutchins, R. O.; Learn, K.; Fulton, R. P. *Tetrahedron Lett.* **1980**, *21*, 27. (b) Keinan, E.; Greenspoon, N. *Tetrahedron Lett.* **1982**, *23*, 241.
(15) (a) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619. (b) Bäckvall, J. E.; Björkman, E.; Petterson, L.; Siegbahn, P. *J. Am. Chem. Soc.* **1984**, *106*, 4369. (c) Nordberg, R. E.; Bäckvall, J. E. *J. Organomet. Chem.* **1985**, *285*, C24. (d) Bäckvall, J. E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892.
(16) (a) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 3435.
(17) On prolonged reaction time, isomerization to the trans isomer occurred.



cis-**10**

chlorophosphonium salt was treated with silver triflate in chloroform to give *cis*-**7**. Comparison of the NMR spectrum of this compound with that of the organic products observed from the stoichiometric reaction of **4** with PPh_3 discussed above confirmed the structures assigned for **7**.

To eliminate the possibility of triflate migration from the (π-allyl)palladium triflate complexes as a pathway for isomerization, we studied the corresponding reaction of π-allyl complex *cis*-**11**[18a] with PPh_3. Rapid isomerization took place, confirming that the triflate is not responsible for the isomerization.[18b]



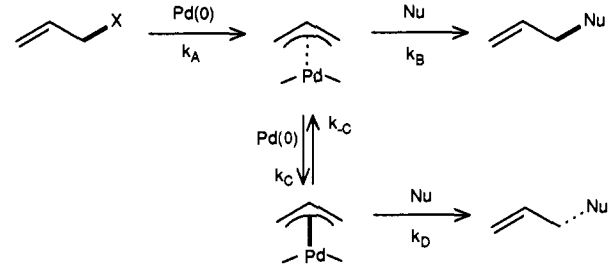
cis-**11**

D. Effect of Ligand. Murahashi recently reported[19] that the stereospecificity in Pd(0)-catalyzed azidations of **1c** in THF/H_2O was critically dependent on the nature of added ligand, bidentate ligands being superior to PPh_3. We therefore studied the effect of dppe (1,2-bis(diphenylphosphino)ethane) in the Pd(0)-catalyzed nucleophilic substitution of *cis*-**1c**. Our results show that the use of $Pd(dppe)_2$ as the catalyst led to a highly stereospecific reaction with $NaCH(CO_2Me)_2$, $NaCH(SO_2Ph)_2$, and Et_2NH (entries 3, 6, and 9, Table III). The results from the latter two nucleophiles are of particular interest since the corresponding reactions with $Pd(PPh_3)_4$ as catalyst are nonstereospecific[3a,b,4] (entries 7 and 10, Table III). Also, the isomerization of the starting material observed in the $Pd(PPh_3)_4$-catalyzed amination (entry 10, Table III) was inhibited by the use of $Pd(dppe)_2$ as the catalyst (entry 9, Table III).

Discussion

Oxidative addition of Pd(0)–phosphine complexes to allylic substrates to give π-allyl complexes has been established to proceed with inversion of configuration after prior anticoordination to the olefinic double bond.[16] Subsequent nucleophilic attack on the (π-allyl)palladium complex leads to the organic product. Depending on the nature of the incoming nucleophile, attack occurs either on the metal or on the coordinated π-allyl.[13,14] Stabilized carbon nucleophiles, amines, and most oxygen nucleophiles react with overall retention while carboxylates show borderline behavior. The use of allylic carboxylates can thus lead to anomalous inversion products, which can be explained by a coordination of acetate to palladium after initial oxidation addition followed by migration of the acetate to the π-allyl (probably via a σ-allyl)[20] leading to isomerization of starting material. Our previously reported results,[4] together with the results presented in Table III, where no isomerization of the starting material **1c** (X = OAc) was observed, exclude this pathway as a likely explanation for the loss of stereospecificity in alkylation reactions involving sodium as the counterion.[21] The experiments in entries 7 and 8, Table III, where

Scheme IV



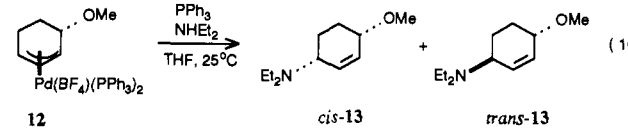
cis-**1c** and *trans*-**1c**, respectively, gave products via nonstereospecific reactions without any detectable isomerization of the starting materials, are particularly convincing in this respect. Previously the loss of stereospecificity of this reaction was explained by isomerization of the starting material.[3b,6]

The isomerization of allylic acetates observed in the Pd(0)-catalyzed diethylamination[4,15c] can be completely inhibited by the addition of small amounts of LiCl, but this only partly improves the stereospecificity of the catalytic reaction.[4] The remaining loss of stereospecificity is again best explained by a Pd–Pd displacement.

The fact that isomerization of **6** occurs with added $Pd(PPh_3)_4$ at −15 °C (Table I, Scheme II) provides strong support for the hypothesis that free Pd(0) is sufficiently nucleophilic to isomerize (π-allyl)palladium intermediates via an S_N2-type attack (Scheme IV, step C). The isomerization of (π-allyl)palladium complexes observed on addition of only PPh_3 is also consistent with this mechanism since the PPh_3 attack on the (π-allyl)palladium complex produces an allylphosphonium salt and Pd(0) of which the latter would account for the isomerization. The established trans attack by phosphine on the π-allyl group eliminates the possibility that isomerization is caused by a cis attack of PPh_3 on the (π-allyl)palladium complexes and subsequent oxidative addition of Pd(0). The only pathway for the PPh_3-induced isomerization therefore seems to be that via PPh_3 attack on the allyl group to release the Pd(0) necessary for isomerization. The fact that $Pd(PPh_3)_4$ causes isomerization at −15 °C but PPh_3 does not (Scheme II; Table I, entry 3 versus 6) clearly shows that the isomerization process, i.e., palladium(0) displacing palladium in the π-allyl, is much faster than nucleophilic attack by PPh_3 on the π-allyl group. This would seem to contradict the results of eqs 8 and 9, where a stereospecific reaction takes place in the catalytic reaction where $Pd(PPh_3)_n$ is present. A likely explanation for this phenomenon is that the active Pd(0) catalyst concentration is kept low in the catalytic reaction (eqs 8 and 9) by fast consumption of Pd(0) by the allylic substrates *cis*- and *trans*-**1b**, respectively. This is in line with our previous results.[4]

The effect of the bidentate phosphine dppe as ligand is remarkable in several respects. The increased stereospecificity is best explained by a significantly slower Pd–Pd displacement in the π-allyl intermediates relative to the reaction steps of the catalytic reaction.[22] The negligible isomerization of the starting material *cis*-**1c** in the amination reaction at low conversion when dppe was employed as ligand (Table III, compare entries 9 and 10) can be explained by a faster amination but also by the strong bidentate coordination, which would hinder coordination of acetate and, thus, cis migration.

We are now in a position to give a likely explanation of the previously reported observation of anomalous product *trans*-**13** in the stoichiometric reaction of (π-allyl)palladium complex **12** with Et_2NH in the presence of excess PPh_3 (eq 10).[23] The relative



12 *cis*-**13** *trans*-**13** (10)

(18) (a) The complex *cis*-**11** was prepared from *cis*-**3** by stirring with 1 equiv of PPh_3 and 1 equiv of $AgBF_4$ per palladium followed by addition of another equiv of PPh_3. (b) Control experiments showed that addition of 1 equiv of lithium triflate to *cis*-**6** in THF did not lead to an observable rate enhancement (or decrease) for these processes.

(19) Murahashi, S. I.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, *54*, 3292.

(20) Grennberg, H.; Langer, V.; Bäckvall, J. E. *J. Chem. Soc., Chem. Commun.* **1991**, 1190.

(21) The use of the sodium salt of the nucleophile most likely leads to precipitation of sodium acetate, which as a consequence will be inaccessible to palladium.

(22) Prelimary experiments on the Pd–Pd displacement with dppe as a ligand indicate that this is a slow process: Granberg, K. Unpublished results.

amount of *trans*-**13** was found to increase with the amount of added phosphine. An explanation for this effect can be found in the experimental procedure, which involved addition of PPh_3 to a THF solution of **12** followed by 5 min of stirring at room temperature prior to the addition of amine. Given the results presented above (see also Scheme III) regarding PPh_3-induced isomerization of (π-allyl)palladium complexes, isomerization of **12** will take place as the ratio PPh_3Pd becomes larger than 2. The extent of isomerization will be dependent on the concentration of Pd(0), which in turn depends on the amount of added PPh_3 that can act as an external nucleophile to produce Pd(0).

The Pd(0)-catalyzed nucleophilic substitution of allylic substrates involves two important steps: (i) oxidative addition of Pd(0) to the allylic substrate and (ii) attack by the nucleophile on the intermediate (π-allyl)palladium complex (Scheme IV). If the oxidative addition step is rate limiting ($k_A \ll k_B \sim k_D$, common for allylic acetates in combination with reactive nucleophiles), there will be a considerable amount of Pd(0)–phosphine complex in the reaction mixture since it is consumed much more slowly than it is produced. If attack by Pd(0) on the intermediate is faster than attack by the nucleophile ($k_C \sim k_{-C} \gg k_B \sim k_D$), complete isomerization will result. If the nucleophile is sterically demanding ($NaCH(SO_2Ph)_2$, e.g.), or if the approach for nucleophilic attack is hindered (see ref 3e), a situation where nucleophilic attack becomes rate limiting will be at hand (i.e., $k_A \gg k_B \sim k_D$). This will increase the lifetime of the (π-allyl)palladium intermediate and thereby also increase the possibility for Pd(0) to attack, and thus isomerize, the intermediate. The concentration of Pd(0)–phosphine complex can, however, be dramatically reduced by the use of very reactive allylic substrates ($k_A \gg k_C \sim k_{-C}$) which would drain Pd(0) from the reaction mixture.[4] The latter situation gives a likely explanation as to why the synthesis of phosphonium salts **10** from **1b** is stereospecific (i.e., poor nucleophile and excellent leaving group).

In a catalytic reaction the degree of isomerization via the mechanism depicted in Scheme IV will depend on the arithmetical product [Pd(0)][(π-allyl)Pd].[4] The increased isomerization observed when the amount of catalyst is increased (Table III, entry 1 versus 2 and 3 versus 4) therefore gives further support to a mechanism in which Pd(0) displaces palladium. A similar effect was reported by Tsuji,[5a] who observed that an increased concentration of $Pd(PPh_3)_4$ in intramolecular alkylations of acyclic chiral acetates led to an increased loss of chirality transfer.

Conclusion

We have demonstrated that (π-allyl)palladium complexes do isomerize by a mechanism involving nucleophilic trans attack by palladium(0)–phosphine complexes in a number of solvents, and that the rate of this process accounts for the isomerization observed in catalytic reactions of allylic substrates. The isomerization due to Pd–Pd displacement can be inhibited by the use of (i) a reactive allylic substrate, (ii) a low Pd(0) concentration, and (iii) a bidentate ligand. These results explain several cases of stereorandomization in Pd(0)-catalyzed reactions, and they should find application in the search for methods of how to avoid isomerization and thus improve the use of an important synthetic method.[1,2]

Experimental Section

NMR spectra were obtained with a Varian XL 300 FT spectrometer, ^1H NMR at 299.3 MHz, ^{31}P NMR at 121.4 MHz, and $^{13}C\{^1H\}$ NMR at 75.4 MHz. DEPT and REYCOR techniques were used for ^{13}C NMR and ^1H NMR assignments. ^{13}C spectra are reported with the middle peak of $CDCl_3$ (77.00 ppm) as internal reference while tetramethylsilane (TMS) was used as reference for ^1H NMR spectra. ^{31}P NMR spectra were referenced to external H_3PO_4 (85% in D_2O). Infrared spectra were recorded with a Perkin-Elmer 1600 FT-IR spectrometer. Analytical GLC was performed on a Varian 3400 gas chromatograph using a 30-m DB5 capillary column. Tetrahydrofuran (THF) was distilled from a deep blue potassium benzophenone ketyl solution; benzene, chloroform, and methylene chloride were distilled from calcium hydride. Bis(phenylsulfonyl)methane, dimethyl malonate, diethylamine, and deuterated solvents were all purchased from Aldrich and used without further purification. Compounds **1** (**a**–**c**),[4] bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$) and tris(dibenzylideneacetone)palladium(0) ($Pd_2(dba)_3$),[7b] tetrakis(triphenylphosphine)palladium(0),[24] and bis(μ-chloro)bis[4-methoxy(1,2,3-η)-cyclohexenyl]dipalladium (**8**)[23] were prepared according to literature procedures. The sodium salts of bis(phenylsulfonyl)-methane, diethyl malonate, and dimethyl malonate were prepared from stoichiometric amounts of sodium hydride and substrate in THF and stored under dry nitrogen in a desiccator.

Bis(μ-chloro)bis[5-carbomethoxy-(1,2,3-η)-cyclohexenyl]dipalladium (3). The trans complex was synthesized following an earlier reported procedure[7b] using Kurosawa's recent observations on the reaction's solvent dependence,[7a,8] while the cis complex was synthesized in a slightly different manner.[8]

***cis*-3.** $Pd(dba)_2$ (575 mg, 1.00 mmol) and *trans*-**1a** (175 mg, 1.00 mmol, 98% trans) were stirred in DMSO (10 mL) for 2 h (yellow-green solution). Water (15 mL) and chloroform (20 mL) were added to the stirred reaction mixture. The organic phase was separated, washed with water (3 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo to give a yellow solid. Flash chromatography on silica (CH_2Cl_2, then $CHCl_3$) afforded the complex as light yellow crystals in 95% yield (96% cis). Spectroscopic data were in accordance with those reported.[7a]

***trans*-3.** $Pd_2(dba)_3C_6H_6$ (328 mg, 0.330 mmol) and *trans*-**1a** (115 mg, 0.659 mmol, 96% trans) were stirred in benzene (7 mL) for 22 h and then worked up and purified as above: yield 82% (92% trans). Spectroscopic data were in accordance with those reported.[7a]

Bis[μ-[(trifluoromethyl)sulfonyl]oxy]bis[5-carbomethoxy-(1,2,3-η)-cyclohexenyl]dipalladium (4). Both isomers were obtained by using the same procedure.

***cis*-4.** Complex *cis*-**3** (752 mg, 1.34 mmol) was dissolved in distilled methylene chloride (50 mL), and silver trifluoromethanesulfonate (722 mg, 2.81 mmol) was added in one portion. The mixture was stirred for 1 h and then concentrated in vacuo to 5 mL followed by filtration through a short Celite plug. Removal of the solvent in vacuo followed by high-vacuum pumping for several hours gave 1.04 g (98%, 96% cis) of a pale brown-yellow semisolid. This complex is quite hygroscopic and rather unstable at 20 °C and is therefore best stored under dry nitrogen in the freezer: IR (CH_2Cl_2) 1733, 1678, 1448, 1438, 1419, 1306, 1210, 1022, and 636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.73 (t, J = 7 Hz, 1 H, H-2), 5.33 (t, J = 7 Hz, 2 H, H-1 and H-3), 3.70 (s, 3 H, CH_3), 2.24–2.03 (m, 3 H, H-5 and H_{ax}-4), 1.89 (dd, 2 H, J = 18, 10 Hz, H_{eq}-4); ^{13}C NMR ($CDCl_3$) δ 175.1, 119.1 (q, J = 319 Hz), 102.6, 74.8, 52.3, 35.3, 31.4.

***trans*-4**: obtained as a semisolid in 98% yield from *trans*-**3** (93% trans); IR (CH_2Cl_2) 1733, 1436, 1307, 1220, 1209, 1020, and 636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (t, J = 7 Hz, 1 H, H-2), 5.28 (m, 2 H, H-1 and H-3), 3.66 (s, 3 H, CH_3), 3.24 (quint, J = 7 Hz, 1 H, H-5), 2.14 (ddd, 2 H, J = 18, 7, 3 Hz, H_{ax}-4), 1.75 (ddd, 2 H, J = 18, 7, 4 Hz, H_{eq}-4); ^{13}C NMR ($CDCl_3$) δ 173.9, 119.5 (q, J = 318 Hz), 101.8, 75.8, 52.2, 37.5, 29.6.

Bis[1,2-bis(diphenylphosphino)ethane]palladium(0).[25] Dppe (1.18 g, 2.96 mmol) was added to a stirred mixture of $Pd_2(dba)_3CHCl_3$ (729 mg, 0.704 mmol) in degassed benzene (20 mL) under dry N_2. The initial dark-red color changed to brown-yellow after 5 min, and stirring was continued for 1 h. The solvent was removed in vacuo to give a yellow solid, which was treated with ice-cold degassed acetone, and the resulting slurry was cannulated into a Schlenk filtration device. Washing with cold acetone (total 120 mL) gave, after drying to constant weight, a bright yellow solid (76% yield). The solid complex was surprisingly air stable but decomposed rapidly in solution if air was introduced; it is best stored cold under dry N_2.

Determination of Rates and Equilibrium Constants by NMR Spectroscopy. Solvents used in NMR studies were degassed before use and were transferred via syringe. The palladium complex (**4**) was first dissolved and then cooled (−78 °C) before the addition of the appropriate phosphine ligand. Minimum heating to dissolve the added ligand was followed by recooling. Addition of any desired additive such as Pd(0) complexes and/or phosphines was followed by slight heating to obtain a solution. Collection of data was performed at regular intervals in blocks of 16 transients, which were Fourier transformed and integrated. This was continued until no significant change could be detected. ^1H NMR spectroscopy was used in the collection of data in $CDCl_3$ while ^{31}P NMR spectroscopy was conveniently used for monitoring the reaction in other solvents. Referencing and locking of samples with undeuterated THF were conveniently done by immersing a small sealed capillary (Varian) containing the deuterated reference.

(23) Bäckvall, J. E.; Nordberg, R. E.; Zetterberg, K.; Åkermark, K. *Organometallics* **1983**, *2*, 1625.

(24) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676.

(25) See also: (a) Chatt, J.; Hart, F. A.; Watson, H. R. *J. Chem. Soc.* **1962**, 2537. (b) Verkade, J. G.; Mason, M. R. *Organometallics* **1990**, *9*, 864.

[[(Trifluoromethyl)sulfonyl]oxy](triphenylphosphine)[5-carbomethoxy-(1,2,3-η)-cyclohexenyl]palladium (5). ***cis*-5**: IR ($CDCl_3$) 3061, 2954, 1731, 1437, 1307, 1232, 1208, 1179, 1016, 696, 636, 527, and 510 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.58–7.40 (m, 15 H, aromatic), 6.40 (d br t, J = 7, 6 Hz, 1 H, H-1), 5.86 (br t, J = 6 Hz, 1 H, H-2), 4.14 (apparent br q, 1 H, H-3), 3.63 (s, 3 H, CH_3), 2.69 (m, 1 H, H-4), 2.35 (ddd, J = 19, 11, 6 Hz, 1 H, H-4), 2.02 (tt, J = 11, 5 Hz, 1 H, H-5), 1.79 (m, 1 H, H-6), 1.41 (ddd, J = 19, 11, 5 Hz, 1 H, H-6); ^{31}P NMR δ ($CDCl_3$, 23.1), (THF, 24.8), (C_6D_6, 24.7), (CD_3CN, 26.5), ((CD_3)$_2$CO, 26.1), ((CD_3)$_2$SO, 24.4).

***trans*-5**: IR ($CDCl_3$) 3061, 2954, 1731, 1437, 1307, 1232, 1208, 1179, 1016, 696, 636, 527, and 510 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56–7.41 (m, 15 H, aromatic), 6.25 (m, 1 H, H-3), 5.81 (m, 1 H, H-2), 4.15 (m, 1 H, H-1), 3.61 (s, 3 H, CH_3), 3.17 (quint, J = 7 Hz, 1 H, H-5), 2.66 (m, 1 H, H-4), 2.26 (m, 1 H, H-4), 1.43 (m, 1 H, H-6), 1.31 (m, 1 H, H-6); ^{31}P NMR δ ($CDCl_3$, 23.0), (THF, 24.0), (C_6D_6, 22.9), (CD_3CN, 25.9), ((CD_3)$_2$CO, 25.8), ((CD_3)$_2$SO, 24.1).

Bis(triphenylphosphine)[5-carbomethoxy-(1,2,3-η)-cyclohexenyl]palladium Trifluoromethanesulfonate (6). ***cis*-6**: IR ($CDCl_3$) 2972, 1654, 1464, 1232, 1190, 1011, 642, 527, 513, and 500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43–7.22 (m, 30 H, aromatic), 6.38 (t, J = 7 Hz, 1 H, H-2), 5.11 (br t, J = 6 Hz, 2 H, H-1 and H-3), 3.59 (s, 3 H, CH_3), 2.01–1.89 (m, 3 H, H_{eq}-4 and H-5), 1.18 (dt, J = 18, 10 Hz, 2 H, H_{ax}-4); ^{31}P NMR δ ($CDCl_3$, 22.2), (THF, 23.4), (C_6D_6, 23.0), (CD_3CN, 24.0), ((CD_3)$_2$CO, 23.9), ((CD_3)$_2$SO, 23.6).

***trans*-6**: IR ($CDCl_3$) 3060, 1731, 1480, 1436, 1264, 1165, 1097, 1031, 694, 636, 531, 520, 508, and 493 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44–7.21 (m, 30 H, aromatic), 6.20 (t, J = 7 Hz, 1 H, H-2), 5.06 (m, 2 H, H-1 and H-3), 3.61 (s, 3 H, CH_3), 2.68 (tt, J = 9, 6 Hz, 1 H, H-5), 1.71 (m, 2 H, H_{ax}-4), 1.21 (dm, J = 17 Hz, 2 H, H_{eq}-4); ^{31}P NMR δ ($CDCl_3$, 21.3), (THF, 22.7), (C_6D_6, 22.1), (CD_3CN, 23.4), ((CD_3)$_2$CO, 23.4), ((CD_3)$_2$SO, 23.1).

Bis(triphenylphosphine)[4-methoxy-(1,2,3-η)-cyclohexenyl]palladium Trifluoromethanesulfonate (9). ***trans*-9** (in mixture with ***cis*-11**): ^1H NMR ($CDCl_3$) δ 7.48–7.18 (m, 30 H, aromatic), 6.16 (t, J = 7 Hz, 1 H, H-2), 5.19 (m, 1 H, H-1), 5.00 (m, 1 H, H-3), 2.87 (s, 3 H, Me), 2.52 (m, 1 H, H-4), 1.72 (m, 1 H, H-5), 1.57 (m, 1 H, H-6), 1.19 (m, 1 H, H-5), 0.93 (m, 1 H, H-6).

***cis*-9** (in mixture with ***tranas*-11**): ^1H NMR ($CDCl_3$) δ 7.48–7.18 (m, 30 H, aromatic), 6.26 (t, J = 7.1 Hz, H-2), 5.35 (m, 1 H, H-1), 5.19 (m, 1 H, H-3), 2.77 (s, 3 H, Me), 2.52 (m, 1 H, H-4), 1.72 (m, 1 H, H-5), 1.36 (m, 1 H, H-5), 1.19 (m, 1 H, H-6), 0.44 (m, 1 H, H-6).

5-Carbomethoxy-3-(triphenylphosphino)cyclohexene Trifluoroacetate (10). ***trans*-10.** $Pd(PPh_3)_4$ (58 mg, 0.050 mmol) was added to a stirred solution of PPh_3 (288 mg, 1.10 mmol) and ***trans*-1b** (252 mg, 1.00 mmol, 96% trans) in chloroform (2.5 mL) under N_2. The solvent was removed in vacuo after 19 h, and the resulting yellow oil was treated first with ether followed by careful addition of chloroform in order to dissolve the oil without dissolving the $Pd(PPh_3)_2Cl_2$ (bright yellow solids).[26] After the liquid was decanted, more ether was added to the organic solution and an oil precipitated. The liquid layer was decanted again, and the remaining oil was washed twice with ether. High-vacuum pumping gave the product as a white foam, 417 mg (81%, 94% trans): IR (neat) 3060, 2846, 1731, 1687, 1439, 1198, 1158, 1111, 817, 798, 752, 724, 716, and 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.94–7.68 (m, 15 H, aromatic), 6.16 (m, 1 H, H-1), 5.70 (m, 1 H, H-2), 5.31 (dm, J = 18 Hz, H-3), 3.64 (s, 3 H, CH_3) 2.63 (m, 1 H, H-4), 2.36 (m, 1 H, H-6), 2.26–2.06 (m, 2 H, H-4 and H-6), 1.88 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$) δ 173.4, 160.2 (q, J = 33 Hz), 134.9 (d, J = 3 Hz), 134.3 (d, J = 12 Hz), 133.3 (d, J = 9 Hz), 130.3 (d, J = 13 Hz), 116.9 (q, J = 297 Hz), 116.8 (d, J = 6 Hz), 116.5 (d, J = 83 Hz), 51.8, 34.4 (d, J = 5 Hz), 28.0 (d, J = 48 Hz), 25.2 (d, J = 3 Hz), 23.7; ^{31}P NMR ($CDCl_3$) δ 24.8.

***cis*-10**: prepared according to the procedure above in 79% yield (96% cis) from ***cis*-1b** (99% cis); IR (neat) 3059, 2845, 1731, 1687, 1439, 1198, 1160, 1111, 818, 798, 724, and 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93–7.65 (m, 15 H, aromatic), 6.07 (m, 1 H, H-1), 5.75 (m, 1 H, H-3), 5.67 (br t, J = 9 Hz, 1 H, H-2), 3.64 (s, 3 H, CH_3), 3.11 (tdd, J = 11, 4, 3 Hz, 1 H, H-5), 2.61 (dm, J = 12 Hz, 1 H, H_{eq}-4), 2.45 (dm, J = 18 Hz, 2 H, H_{eq}-6), 1.95 (m, 1 H, H_{ax}-6), 1.58 (apparent quint, J = 12 Hz, H_{ax}-4); ^{13}C NMR ($CDCl_3$) δ 174.0, 160.3 (q, J = 32 Hz), 134.6 (d, J = 3 Hz), 133.5 (d, J = 9 Hz), 133.2 (d, J = 12 Hz), 130.2 (d, J = 12 Hz), 118.0 (d, J = 6 Hz), 117.1 (q, J = 299 Hz), 116.4 (d, J = 84 Hz), 51.5, 37.2 (d, J = 12 Hz), 30.7 (d, J = 52 Hz), 27.0 (d, J = 3 Hz), 24.4; ^{31}P NMR ($CDCl_3$) δ 26.8.

Procedure for Palladium(0)-Catalyzed Diethylamination of *cis*-1c.[4] To an oven-dried 10-mL one-necked flask, equipped with a septum–inlet adapter (Teflon stopcock), were added $Pd(PPh_3)_4$, ***cis*-1c** (X = OAc) (0.25 mmol), and THF (2.0 mL). The flask was briefly evacuated and filled with nitrogen three times and heated to 50 °C, and then degassed diethylamine (78 μL, 0.75 mmol) was added via syringe to the stirred solution. Analytical samples (0.2 mL) were filtered through a short silica column (ether) prior to GC analysis.

General Procedure for Palladium(0)-Catalyzed Alkylations of *cis*- and *trans*-1c.[4] The procedure above was followed with a few exceptions. $Pd(PPh_3)_4$ (14.4 mg, 0.0125 mmol), allylic compound *cis*- or ***trans*-1c** (0.25 mmol), and $NaCH(SO_2Ph)_2$ or $NaCH(CO_2Me)_2$ (0.50 mmol) in THF (2 mL) were stirred at 50 °C for the appropriate time (Table III). The reaction was quenched with 2 M HCl (5 mL) and extracted with ether (20 mL). The ethereal phase was washed with brine (5 mL) and dried ($MgSO_4$) followed by evaporation in vacuo.

Acknowledgment. We are grateful to the Natural Science Research Council for financial support.

(26) Deal, D.; Zink, J. I. *Inorg. Chem.* **1981**, *20*, 3995.