Novel Syn Oxidative Addition of Allylic Halides to Olefin Complexes of Palladium(0) and Platinum(0)

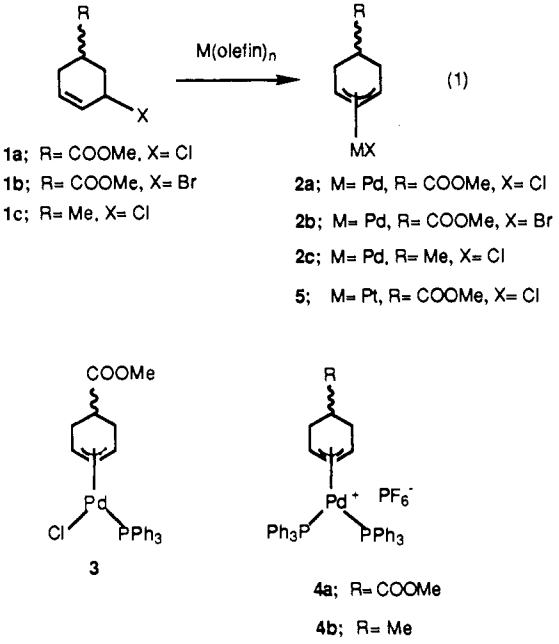
Hideo Kurosawa,* Hiroshi Kajimaru, Sensuke Ogoshi, Hiroto Yoneda, Kunio Miki,† Nobutami Kasai, Shinji Murai, and Isao Ikeda

Contribution from the Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan. *Received April 20, 1992*

Abstract: Stereochemistry of the oxidative addition of 5-(methoxycarbonyl)-2-cyclohexenyl chloride (**1a**) and bromide (**1b**) and 5-methyl-2-cyclohexenyl chloride (**1c**) to palladium(0)–olefin and platinum(0)–olefin complexes to give the corresponding (η^3-allyl)palladium and -platinum complexes was examined as a function of solvent and olefin ligands. Novel syn addition (>90% selectivity) occurred in the reactions of the trans isomers of **1a–c** with palladium complexes containing electron-withdrawing olefinic ligands (maleic anhydride, dimethyl fumarate, fumaronitrile, dibenzylideneacetone) carried out in benzene, CH_2Cl_2, or THF. Somewhat lower syn selectivity (80–43%) was found in the reactions between these palladium complexes and the cis isomer of **1a** or between the analogous platinum complexes and **1a**-trans under the same conditions. Anti oxidative addition dominated in the reactions of **1a**-trans with electron-withdrawing olefin–palladium complexes in acetonitrile or DMSO, or with electron-donating olefin–palladium complexes in benzene or CH_2Cl_2. The crystal structure of Pd(*trans*-(5-methoxycarbonyl)(1-3-η)-cyclohexenyl)(Cl)(PPh_3) was determined. Crystal data: $C_{26}H_{26}O_2ClPPd$, fw = 543.32, monoclinic, space group $P2_1/n$, a = 12.717 (2) Å, b = 9.881 (2) Å, c = 19.772 (3) Å, β = 105.38 (2)°, V = 2395.7 (6) Å^3, Z = 4, D_c = 1.507 g cm^{-3}, R = 0.043 for 4150 reflections ($|F_o| > 3\sigma(|F_o|)$). The six-membered ring adopts a pseudochair conformation, with COOMe occupying the equatorial position. A reaction path for the syn oxidative addition is proposed with the aid of the relative rates of the oxidative addition observed for a series of methyl-substituted allylic chlorides, $ClCHR^1CR^2{=}CR^3R^4$. Cross coupling of **1a** with RBu_3Sn (R = phenyl, vinyl) with net retention of configuration was achieved by the use of a catalyst precursor, $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/maleic anhydride. Evidence is given which shows that the catalytic cycle involves two stereoretentive key reactions, namely, oxidative addition of **1a** with Pd(0) and reductive elimination of the (η^3-allyl)palladiums with organotins, both requiring maleic anhydride as an indispensable ligand to palladium.

Oxidative addition of organic electrophiles (e.g., halides, carboxylates) to low-valent transition metal complexes giving rise to organotransition metal compounds is among the most crucial elementary steps which constitute many synthetically important, metal-catalyzed or metal-mediated organic transformations.[1] Stereochemistry about the susceptible sp^3 carbon atom in the oxidative addition usually ends in inversion in the concerted pathway and racemization in the multistep radical pathway.[1] Although the oxidative addition of allylic electrophiles may well be expected to exhibit a more diverse stereochemical pattern in view of the dual stereoselectivity (anti and syn substitution) observed in allylic substitution reactions with nonmetallic nucleophiles,[2] the majority of the allylic oxidative addition reaction reported so far proceed through anti addition[3] with very few examples exhibiting syn addition.[4]

It was thought that syn addition occurs in the reactions of those substrates in which the leaving group X (Scheme I) is capable of coordinating to metallic nucleophiles prior to oxidative addition (X = 2-benzothiazolyloxy, M = Cu^I;[4a] X = $OOCCH_2PPh_2$, M = Pd^0;[4b] X = $OCONR^-$, M = Cu^I).[4d,e] However, these examples were all inferred from catalytic transformations where evidence for the occurrence of the (η^3-allyl)metal complex intermediate was indirect. Furthermore, no details were given concerning other factors which might influence the stereochemical course of the reaction. We report here the realization of the first syn oxidative addition of allylic halides to palladium(0) and platinum(0) complexes[5,6] and the results of a series of experiments aimed at understanding the factors affecting the course of oxidative addition of allylic halides.



Results

Isolation and Characterization of Oxidative Addition Products from 2-Cyclohexenyl Halides and Olefin–Pd(0) Complexes. Treatment of *trans*-5-(methoxycarbonyl)-2-cyclohexenyl chloride (**1a**-trans) in benzene at room temperature with dibenzylideneacetone–Pd(0) complex $Pd_2(dba)_3$ (5 h) or cyclooctadiene(maleic anhydride)–Pd(0) complex Pd(COD)(MA) (0.5 h) led to isolation of a good yield of an isomerically pure (η^3-allyl)palladium chloride

† X-ray structural correspondence to this author at the present address: Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, Japan.

(1) (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 5–5. (b) Yamamoto, A. *Organotransition Metal Chemistry*; John Wiley: New York, 1986; p 226. (c) Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434–442. (d) Osborn, J. A. *Organotransition Metal Chemistry*; Ishii, Y., Tsutsui, M., Eds.; Plenum: New York, 1975; p 65.

(2) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901–1930.

(3) (a) Tseng, C. C.; Yen, S. J.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2892–2895 and references therein. (b) Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833–4840. (c) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063–3066. (d) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767–7768. (e) Trost, B. M.; Verhoeven, T. R. *Ibid.* **1980**, *102*, 4730–4743.

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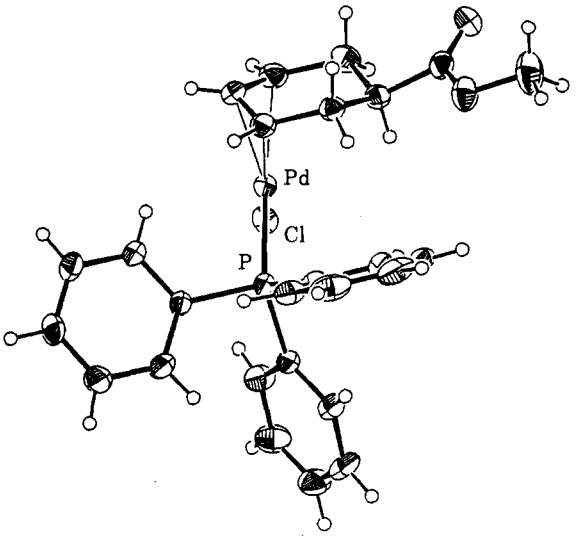
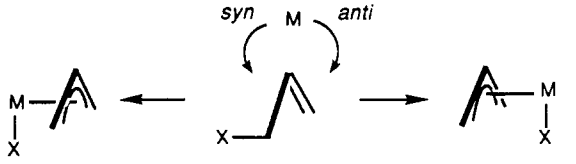


Figure 1. The molecular structure of **3**-trans (ORTEP drawing).[36] Non-hydrogen atoms are represented by thermal ellipsoids at 30% probability levels, whereas hydrogen atoms are drawn as spheres with $B = 1.0$ Å^2.

Scheme I



dimer, **2a**-trans.[7] The crystal structure of **2a**-trans has been determined previously by other workers.[8] We also determined the structure of **3**-trans obtained from **2a**-trans and PPh_3 (Figure 1).

It is seen in Figure 1 that in **3**-trans, as in **2a**-trans,[8] the six-carbon ring adopts a pseudochair conformation bearing the equatorial COOMe substituent trans to the palladium moiety. The hydrogen atom α to COOMe is located close to the palladium moiety, this fact being well reflected in NOE experiments on the bis(phosphine)palladium analogue **4a**-trans obtained by the reaction of **2a**-trans with 2 equiv of PPh_3 and NH_4PF_6; irradiation of the P–Ph ortho protons resulted in considerable enhancement of the intensity of the proton resonance α to COOMe.

Treatment of **1a**-trans with $Pd_2(dba)_3$ or Pd(COD)(MA) *in acetonitrile* resulted in isolation of the cis complex **2a**-cis; **2a**-trans was present in amounts less than 5%. In none of these reactions was trans to cis isomerization of **1a** observed (see, however, the more facile isomerization of **1a**-trans in the case of the platinum complexes described later), nor did the interconversion of **2a**-trans and **2a**-cis occur under the reaction conditions. Furthermore, even in those cases where a mixture of comparable amounts of **2a**-trans and **2a**-cis was obtained by the use of certain solvents or ligands (see below), the product ratio did not change with the reaction time. The cis structure of **2a**-cis was also confirmed previously by X-ray analysis.[8] In the isomer **4a**-cis, derived from **2a**-cis and 2 equiv of PPh_3, no NOE enhancement of the proton resonance α to COOMe was observed upon irradiating the P–Ph ortho protons, as expected from the pseudoboat conformation of **2a**-cis.[8] *trans*-5-(Methoxycarbonyl)-2-cyclohexenyl bromide (**1b**-trans) and Pd(COD)(MA) also underwent syn oxidative addition in benzene and anti addition in acetonitrile, giving the corresponding bromide complexes, **2b**-trans (96% isomeric purity) and **2b**-cis (93% isomeric purity), respectively.

The reaction of the cis isomer of the allylic chloride, **1a**-cis, with $Pd_2(dba)_3$ was sluggish under similar conditions; metallic palladium was gradually deposited before the oxidative addition product was formed. However, Pd(COD)(MA) did react cleanly with **1a**-cis in benzene to give a mixture of the oxidative addition products **2a**-trans and **2a**-cis (25/75). Noteworthy here is the lower degree of syn selectivity than those encountered in the reactions of **1a**-trans.

Oxidative addition of *trans*-5-methyl-2-cyclohexenyl chloride (**1c**-trans) with Pd(COD)(MA) also afforded **2c**-trans (100% isomeric purity) in benzene and **2c**-cis (93% isomeric purity) in acetonitrile. These complexes were characterized by comparison of their ^{1}H NMR spectral patterns with those of **2a**-trans and **2a**-cis. In addition, comparison of NOE experimental results for the cationic complexes **4b**-trans and **4b**-cis with those for **4a**-trans and **4a**-cis was also instructive; irradiating the P–Ph ortho protons resulted in NOE enhancement of the proton resonance α to Me in **4b**-trans but not in **4b**-cis.

Table I. Solvent Effects on Stereoselectivity in Oxidative Addition

allylic chloride	Pd(0) complex	solvent	% syn	% anti
1a-trans	$Pd_2(dba)_3$	benzene	100	0
		CH_2Cl_2	94	6
		THF	95	5
		acetone	75	25
		DMF	29	71
		CH_3CN	5	95
		DMSO	3	97
	Pd(COD)(MA)	benzene	100	0
		CH_2Cl_2	91	9
		THF	93	7
		CH_3CN	4	96
1a-cis	Pd(COD)(MA)	benzene	75	25
		CH_2Cl_2	53	47
		THF	50	50
		CH_3CN	0	100
1b-trans	Pd(COD)(MA)	benzene	96	4
		CH_3CN	7	93
1c-trans	Pd(COD)(MA)	benzene	100	0
		CH_3CN	7	93

Solvent Effect on the Stereochemistry of Oxidative Addition. Stereoselectivity in the oxidative addition of **1a**-trans and **1a**-cis to $Pd_2(dba)_3$ and Pd(COD)(MA) was examined in several solvents (Table I). The selectivity of the reaction changed dramatically with changes in the polarity of the solvent. In the reaction of **1a**-trans, syn oxidative addition dominated in benzene, CH_2Cl_2, and THF, while anti addition dominated in acetonitrile and DMSO. Less selectivity was encountered in acetone and DMF. In the reaction of **1a**-cis, syn selectivity was modest in benzene, CH_2Cl_2, and THF, while exclusive anti addition occurred in acetonitrile.

Ligand Effect on the Stereochemistry of Oxidative Addition. The nature of the ligand bound to Pd(0) affected the stereochemistry of the oxidative addition in a critical way. We first examined how the nature of the olefinic ligand affects the stereochemistry of the oxidative addition shown in eq 1. Table II shows the results of the reactions of **1a**-trans with some isolable olefin–Pd(0) complexes both in the absence and in the presence of additional olefins in CH_2Cl_2, and Table III the results of reactions with olefin–Pd(0) complexes supposed to be generated according to eq 2. While we were not certain of its stoichiometry, we thought that the olefin complex was formed upon treatment of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with 1 equiv of tributyl(phenyl)tin in the presence of the appropriate olefin and that this complex imme-

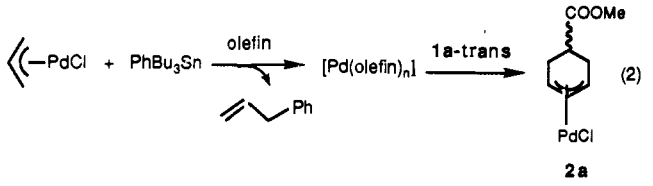
(4) (a) Valverde, S.; Bernabe, M.; Garcia-Ochoa, S.; Gomez, A. M. *J. Org. Chem.* **1990**, *55*, 2294–2298. (b) Stary, I.; Kocovsky, P. *J. Am. Chem. Soc.* **1989**, *111*, 4981–4982. (c) Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670–1672. (d) Goering, H. L.; Kantner, S. S.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 715–721. (e) Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035–1036.

(5) Preliminary communication: Kurosawa, H.; Ogoshi, S.; Kawasaki, Y.; Murai, S.; Miyoshi, M.; Ikeda, I. *J. Am. Chem. Soc.* **1990**, *112*, 2813–2814.

(6) After the publication of our preliminary report,[5] the syn oxidative addition of allylic trifluoroacetates under conditions similar to ours was reported: Vitagliano, A.; Akermark, B.; Hansson, S. *Organometallics* **1991**, *10*, 2592–2599.

(7) For simplicity, the structures of η^3-allyl complexes are written in equations and schemes without regard to the actual association form.

(8) Grennberg, H.; Langer, V.; Bäckvall, J. E. *J. Chem. Soc., Chem. Commun.* **1991**, 1190–1192.



diately reacted with **1a**-trans that had been added prior to the addition of the tin reagent. By this method an almost quantitative yield of **2a** was indeed obtained, its isomeric composition strongly depending on the nature of the olefin added (Table III).

The results in Table III suggest that coordination of the more electron-withdrawing olefin induces higher syn selectivity. This tendency was actually confirmed by the results in Table II for the reactions of Pd(COD)(MA), $Pd(NBE)_2(MA)$ (NBE = norbornene), and $Pd(NBE)_3$, the last complex in particular affording predominantly anti addition product **2a**-cis in both CH_2Cl_2 and toluene.[9] Addition of strongly electron-withdrawing olefins (maleic anhydride, fumaronitrile, dimethyl fumarate) to $Pd(NBE)_3$ increased the syn selectivity. These results revealed that the coordination of electron-withdrawing olefins is essential for syn oxidative addition to occur. The TCNE complex Pd(COD)(TCNE), however, failed to undergo oxidative addition with **1a**-trans even at 50 °C.

It should also be noted here that addition of a large excess of COD, NBE, or styrene to a solution of Pd(COD)(MA) or $Pd(NBE)_2(MA)$ resulted in the formation of considerably higher amounts of the anti addition product **2a**-cis than in their absence (Table II). This result may be ascribed to replacement of the maleic anhydride ligand by these donating olefins to generate anti-addition-directive complexes such as $Pd(COD)_2$ or $Pd(NBE)_3$. Interestingly, however, ^1H NMR measurements of the mixture of Pd(COD)(MA) and COD or that of $Pd(NBE)_2(MA)$ and NBE (each in a 1:10 ratio) showed the presence of very little, if any, free maleic anhydride; the resonance for the coordinated maleic anhydride in Pd(COD)(MA) or $Pd(NBE)_2(MA)$ was somewhat broadened and shifted only slightly to lower field. These results suggest that the palladium(0) complexes having the more donating olefin ligands ($Pd(COD)_2$, $Pd(NBE)_3$ undergo anti oxidative addition considerably faster than Pd(COD)(MA) or $Pd(NBE)_2(MA)$ undergo syn addition. This notion is in line with the failure of Pd(COD)(TCNE) to react with the allylic chlorides described above.

Triphenylphosphine complex $Pd(PPh_3)_4$ reacted with **1a**-trans to give exclusively the anti adduct **3**-cis even in benzene and CH_2Cl_2. Thus, we could provide a direct proof of the anti oxidative addition of $Pd(PPh_3)_4$ implicated in catalytic allyl coupling.[3b] A supposed monophosphine-coordinated Pd(0) species, $Pd(PPh_3)((E)\text{-}MeOOCCH{=}CHCOOMe)_n$, generated from reductive elimination of $Pd(Ar)(\eta^3\text{-}C_3H_5)(PPh_3)$ ($Ar = C_6H_3Cl_2\text{-}2,5$) assisted by dimethyl fumarate,[10] also gave the anti addition product **3**-cis.

A carbonyl complex, $Pd(CO)_n$, is not available under ambient conditions, so we tried to generate a CO-containing Pd(0) species in situ and then allow it to react with **1a**-trans. Thus, when $Pd(\eta^3\text{-}C_3H_5)(acac)$ (acac = acetylacetonate) was treated with CO gas in CH_2Cl_2 in the presence of **1a**-trans, a clean reaction took place, giving rise to a high yield of the anti product **2a**-cis (100% selectivity). It should be noted that this procedure was not applicable in benzene and THF, in which rapid deposition of metallic palladium took place, though we cannot provide any reasonable explanation for this difference.

Stereochemistry of the Oxidative Addition of Platinum(0) Complexes. Reactions of dibenzylideneacetone–Pt(0) complex $Pt(dba)_2$ with **1a**-trans were more sluggish than those of the palladium analog; the yield and the stereoisomeric composition of the oxidative addition product **5** depended on the time of storage of the Pt(0) complex employed. An old sample reacted more slowly, requiring longer reaction periods (>2 days), during which occurrence of partial isomerization of **1a**-trans to **1a**-cis was recognized. Therefore, we estimated the stereoselectivity of the oxidative addition of **1a**-trans to $Pt(dba)_2$ at early stages of the reaction (2 h, ca. 30% conversion) by the use of a freshly prepared sample of the Pt(0) complex. This method showed 43% syn selectivity in the reaction of $Pt(dba)_2$ with **1a**-trans in CH_2Cl_2, a value considerably lower than the selectivity of the reaction of the palladium analog. It should also be noted that addition of 5 equiv of maleic anhydride to the solution of $Pt(dba)_2$ increased the syn selectivity from 43% to 80%.

On the other hand, the reaction of $Pt(NBE)_3$ with **1a**-trans in CH_2Cl_2 was faster, affording predominantly the anti addition product **5**-cis (isomeric purity 93%). Unfortunately, the complex $Pt(NBE)_2(MA)$ failed to react with **1a**-trans under similar conditions. We cannot give the reason for the difference in reactivity between this complex and the complex generated from a mixture of $Pt(dba)_2$ and maleic anhydride described above.

Table II. Stereoselectivity in Oxidative Addition of **1a**-trans with Olefin–Pd(0) Complexes in CH_2Cl_2[a]

complex	additive (equiv/Pd)	% syn	% anti
Pd(COD)(MA)	none	91	9
	styrene (10)	62	38
	COD (10)	58	42
	NBE (10)	58	42
	NBE (100)	38	62
$Pd(NBE)_2(MA)$	none[b]	92	8
	NBE (10)	34	66
$Pd(NBE)_3$	none	7	93
	AN (5)	20	80
	DMF (5)	87	13
	FMN (5)	93	7

[a] Abbreviations: MA, maleic anhydride; COD, 1,5-cyclooctadiene; NBE, norbornene; AN, acrylonitrile; DMF, dimethyl fumarate; FMN, fumaronitrile. [b] The same result was obtained when MA (5 equiv) was added to $Pd(NBE)_3$.

Table III. Stereoselectivity in Oxidative Addition of **1a**-trans with in Situ Generated Olefin–Pd(0) Complexes[a]

olefin[b]	% syn	% anti
NBE	8	92
COD	10	90
AN	33	67
none	45	55
MMA	91	9
MA	95	5
DMM	97	3
DMF	97	3
FMN	97	3

[a] Conditions: $Pd(\eta^3\text{-}C_3H_5)Cl$ 0.01 mmol, $PhBu_3Sn$ 0.009 mmol, olefin 0.05 mmol, **1a**-trans 0.02 mmol in CD_2Cl_2 (0.6 mL). [b] Abbreviations: NBE, norbornene; COD, 1,5-cyclooctadiene; AN, acrylonitrile; MMA, methyl methacrylate; MA, maleic anhydride; DMM, dimethyl maleate; DMF, dimethyl fumarate; FMN, fumaronitrile.

Table IV. Relative Reactivity of Allylic Chlorides $ClCHR^1CR^2{=}CR^3R^4$ with Olefin–Pd(0) Complexes in CH_2Cl_2

complex	R^1	R^2	R^3	R^4	rel rate
Pd(COD)(MA)	H	H	H	H	1
	Me	H	H	H	1.47
	H	Me	H	H	0.22
	H	H	Me[a]	H	0.13
	H	H	Me	Me	0.32
$Pd(NBE)_3$	H	H	H	H	1
	Me	H	H	H	0.33
	H	Me	H	H	0.27
	H	H	Me[a]	H	0.17
	H	H	Me	Me	0.27

[a] *E*-Isomer.

(9) (a) The reactions of $Pd(NBE)_3$ were carried out at low temperatures due to its thermal instability.[9b] It was confirmed that the stereoselectivity of the reaction of Pd(COD)(MA) with **1a** was completely identical in benzene and toluene. (b) Green, M.; Howard, J. K. D.; Spencer, J. L.; Stone, F. G. A. *J. Chem. Soc., Dalton Trans.* **1976**, 271–277.

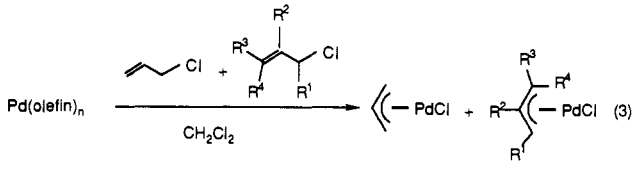
(10) Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333–6340.

Table V. Stereoselectivity in Cross Coupling of **1a** with RBu_3Sn Catalyzed by Maleic Anhydride–Palladium Complex[a]

allylic chloridie	R	solvent	% syn	% anti
1a-trans	Ph	benzene	96	4
		CH_2Cl_2	92	8
		THF	97	3
		CH_3CN	0	100
	vinyl	benzene	92	8
		CH_2Cl_2	90	10
		CH_2Cl_2[b]	4	96
		THF	97	3
		CH_3CN	0	100
1a-cis	Ph	benzene	67	33
	vinyl	benzene	72	28
		CH_2Cl_2	53	47

[a] At 25 °C for 48 h with **1a** (0.4 mmol) and RBu_3Sn (0.4 mmol) in 3 mL of solvent. Catalyst precursor: $Pd(\eta^3\text{-}C_3H_5)Cl$ (5 mol %) and maleic anhydride (20 mol %). NMR yields were 80–90% for **1a**-trans and 40–50% for **1a**-cis. [b] 1,5-Cyclooctadiene (20 mol %) was used instead of maleic anhydride.

Relative Reactivity of Some Substituted Allylic Chlorides. To examine the effect that substituents on allylic chlorides have on the rate of oxidative addition, the relative reactivity order of some substituted allylic chlorides was determined by examining the relative amount of two η^3-allylic complexes formed from the reaction of Pd(COD)(MA) or $Pd(NBE)_3$ with an equimolar mixture of two allylic chlorides in CH_2Cl_2 (eq 3) (Table IV). One

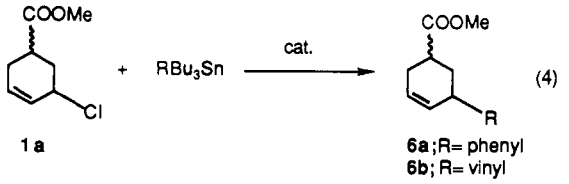


(3)

series of experiments always employed unsubstituted allyl chloride as one component, while in the other series these results were counterchecked by the use of a mixture of two allylic chlorides other than the unsubstituted one. The results from these two series of experiments agreed with each other within experimental error.

In line with the results obtained previously in the reaction of Ir(I) complexes with substituted allylic chlorides,[11] introduction of the methyl substituents at the C=C carbons decreased the reaction rate. However, very notable in Table IV is the higher reactivity of the α-methyl-substituted substrate than of the unsubstituted one in the reaction with Pd(COD)(MA), while the reversed order of reactivity was observed with $Pd(NBE)_3$. The higher reactivity of the γ,γ-dimethyl-substituted substrate than of the γ-methyl-substituted one in the reactions of both complexes may also be noteworthy when compared to the remarkable retardation effect of γ-substituents in the S_N2' oxidative addition of allylic thiolates to $Pd(PR_3)_2$.[12]

Stereochemistry of Oxidative Addition during Catalytic Cross Coupling. We examined whether the syn stereoselectivity of the oxidative addition of allylic chlorides to Pd(0) complexes can be applied to a catalytic cross-coupling reaction. Thus, **1a** was reacted with RBu_3Sn (R = phenyl, vinyl) in various solvents by the use of a catalyst precursor, $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/maleic anhydride (eq 4) (Table V).

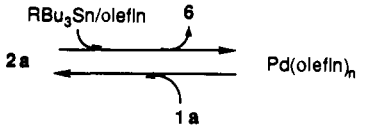


(4)

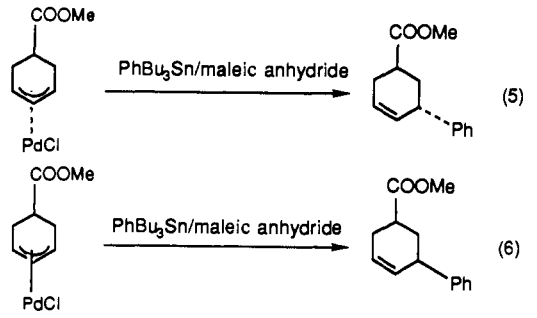
1a **6a**; R = phenyl **6b**; R = vinyl

Both phenylation and vinylation of **1a**-trans proceeded cleanly with overall retention of configuration in benzene, CH_2Cl_2, and THF, and with overall inversion in acetonitrile if maleic anhydride was used as a cocatalyst. In the absence of maleic anhydride, however, phenylation in benzene was too slow to give a good yield of coupling product **6a**, and vinylation, while faster than phenylation, gave coupling product **6b** with only 70% retention of configuration. The phenylation and vinylation of **1a**-cis were slower than those of **1a**-trans even in the presence of maleic anhydride, and the selectivity for retention was lower in each case (see Table V). It is thus evident from these results that the stereochemical trends in the catalytic cross coupling of **1a**-trans and **1a**-cis in Table V well reflect those in the stoichiometric oxidative addition as long as maleic anhydride is present in both reaction systems.

Scheme II



The initial step of the catalysis may be written as in eq 2. We also found that the reaction of each of **2a**-trans and **2a**-cis with $PhBu_3Sn$ afforded good yields of **6a** with almost 100% syn stereoselectivity[13] when maleic anhydride was present in the reaction mixture (eqs 5 and 6).[14] However, in the absence of maleic anhydride, **2a**-trans reacted with $PhBu_3Sn$ more slowly, with benzene, biphenyl, and 4-methoxycarbonylcyclohexene being produced as byproducts. Furthermore, the reaction of **2a**-cis with $PhBu_3Sn$ in the absence of maleic anhydride was even more sluggish and gave very low yields of **6a** consisting of both isomers.



(5)

(6)

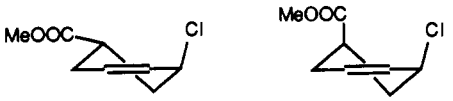
^1H NMR measurement of the catalytic reaction mixture **1a**-trans/$PhBu_3Sn$ with the use of a somewhat higher concentration of the catalyst precursor $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/maleic anhydride confirmed that almost all of the palladium species detectable by NMR spectroscopy exists in the form of **2a**-trans in the whole course of the catalysis. Thus, we propose that it is the reaction of **2a** with the tin reagents to give the coupling products and the Pd(0) complex (Scheme II) that is the turnover-determining step.[15]

Discussion

Stereochemical Diversity in Oxidative Addition of Allylic Halides. The present study demonstrated that the stereochemistry of the oxidative addition of allylic halides to palladium(0) and platinum(0) complexes is more diverse than has been imagined before, being affected in particular by the nature of the reaction solvent and the metal-bound ligand group. The novel syn addition is favored by nonpolar solvents and electron-withdrawing olefinic ligands. Significantly, lack of either of these two requirements shifted the selectivity to anti addition. The different degree of syn selectivity in the reactions of **1a**-trans and **1a**-cis in nonpolar solvents (Table I) may be traced to a steric effect. That is, the lower syn selectivity with **1a**-cis arose because oxidative addition

(11) Pearson, R. G.; Poulos, A. T. *Inorg. Chim. Acta* **1979**, *34*, 67–76.
(12) Osakada, K.; Chiba, T.; Nakamura, Y.; Yamamoto, T.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1589–1591.
(13) Hayashi, T.; Konishi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1984**, 107–108.
(14) (a) Goliaszewski, A.; Schwartz, J. *Tetrahedron* **1985**, *41*, 5779–5789 and references therein. (b) Temple, J. S.; Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 1310–1315. (c) Hayasi, Y.; Riediker, M.; Temple, J. S.; Schwartz, J. *Tetrahedron Lett.* **1981**, *22*, 2629–2632.
(15) It was also confirmed recently that transmetalation from organotins to organopalladium halides and triflates is the overall turnover-determining step of the Pd-catalyzed cross-coupling reactions.[16]
(16) Farrina, V.; Krishman, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595.

most probably requires the susceptible C–Cl bond to lie nearly parallel to the p orbitals of the C=C bond (**7** and **8**);[17] therefore the syn addition may involve greater steric constraints in certain key step(s) (see below) of the reaction of **1a**-cis than that of **1a**-trans.



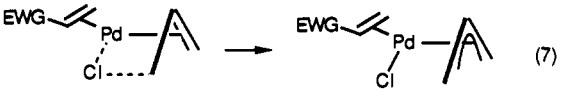
7 **8**

5-(Methoxycarbonyl)-2-cyclohexenyl acetate (both trans and cis isomers) failed to react with Pd(COD)(MA) or $Pd_2(dba)_3$ under the conditions for syn addition. Note, however, the recent finding[6] that some allylic trifluoroacetates did undergo syn oxidative addition with $Pd(dba)_2$ in THF and anti addition in THF/acetonitrile. The above acetate was reported[18] to undergo cross coupling with organotins catalyzed by $Pd_2(dba)_3$ in DMF with net inversion of configuration, suggesting anti oxidative addition of the acetate in this solvent.

It should also be pointed out here that interpretation of the stereochemical results obtained from a cyclohexenyl system must often take into account a conformational bias;[2] the syn attack of a nucleophile at the γ-carbon (S_N2' path) in the conformation having a pseudoaxial leaving group (as in **7** and **8**) leads to a half-chair-like product more stable than the boat-like one to which anti attack leads. However, it is not certain how crucial this bias is in the reaction of metallic nucleophiles which might take a different course.[19] No matter how large the degree of the steric bias for syn addition with the cyclohexenyl system may be, the dramatic switching of the stereochemistry of oxidative addition by the choice of solvents and ligands most probably is a consequence of the change in the electronic requirements for the transition state, as explained below.

Reaction Path of Syn Oxidative Addition. On the basis of the solvent and ligand effects on stereoselectivity (Tables I–III) and the substituent effect on the reaction rate (Table IV), we propose a possible pathway for the novel syn oxidative addition of allylic halides. The initial step of the oxidative addition, under either syn or anti addition conditions, would be coordination of the C=C part of the substrate to the metal.[19] The coordination of allylic halides to molybdenum and tungsten prior to oxidative addition has been confirmed spectroscopically.[20] The decrease in the relative reaction rate upon methyl substitution at the C=C carbons (Table IV) is consistent with this C=C bond coordination. In the case of the reaction with $PdL_2(MA)$ (L = $^1/_2$COD, NBE), the substrate can replace either L or MA. We believe it is almost exclusively L that is replaced, for this is consistent with the stereoelectronic origin of the intensified metal–olefin π back bond interaction in trigonal planar palladium(0) and platinum(0) complexes having one withdrawing and two donating olefin ligands.[21] We indeed confirmed by ^{1}H NMR spectroscopy in this study that the equilibrium between [M(NBE)$_3$ + MA] and [M(NBE)$_2$(MA) + NBE] (M = Pd, Pt) lies by far to the latter mixture.

The coordination of the C=C bond to the metal would lead to an electron flow, more or less, from metal to substrate through π back-bonding, thereby making the substrate more susceptible to C–Cl bond heterolysis. In the reactions of complexes bearing only electron-donating ligand groups, the substrate-bound metal center may be sufficiently nucleophilic to attack the α-carbon atom leading to inversion of configuration at this carbon (the modified S_N2 path).[11] Even in the reactions of complexes bearing withdrawing ligands, the polar solvent would help stabilize the transition state of such an anti addition step which involves a large charge separation. However, this efficient charge separation would not be expected to occur so readily in the reactions of complexes having electron-withdrawing olefins carried out in nonpolar solvents, nor would the complexes possess sufficient nucleophilicity for anti attack. A concerted three-center oxidative addition (syn addition) to the C–Cl bond may also be quite a high energy process. We propose that the C–Cl bond cleavage in this case possesses partial S_N1 character, being assisted by the chelate coordination of the Cl atom and the C=C part to the metal atom bearing a considerably high positive charge, leading to syn oxidative addition (eq 7).



(7)

The uniquely higher reactivity of the α-methyl-substituted allylic chloride than of the unsubstituted one in reactions with Pd(COD)(MA) under syn addition conditions (Table IV) supports the partial S_N1 character of the C–Cl bond cleavage. On the other hand, the reversed reactivity order in reactions with Pd(NBE)$_3$ is consistent with the S_N2 (modified) character of the C–Cl bond cleavage. The syn stereochemical course, driven by the precoordination of the leaving group (Cl), is similar to that driven by P–Pd and N–Cu interactions in the oxidative addition of the substrates containing leaving group $OOCCH_2PPh_2$, 2-benzothiazolyloxy, or $OCONR^-$.[4a,b,d,e] Unfortunately, we obtained no spectral evidence for the occurrence of a Cl–Pd interaction in the rapid reaction of Pd(COD)(MA) with CH_2=$CHCH_2Cl$ in CD_2Cl_2 even at −50 °C, nor was any indication of the interaction between this complex and propyl chloride observed at room temperature. For an effective Cl–Pd interaction to take place during oxidative addition, it seems essential for the metal atom not to move in the direction of the allylic γ-carbon, but rather to remain sitting on the C=C bond. Thus, the formation of a discrete η^1-allylic intermediate seems less likely.

We cannot completely exclude an alternative explanation for the syn addition path, namely, an S_N2' step[2,22] in which the Pd atom would attack directly at the γ-carbon without prior coordination of the substrate C=C bond. The distortion of LUMO in the allylic system has been said to be favorable for the syn S_N2' process.[22b] However, the anti S_N2' path has also been predicted to be feasible theoretically[22b,c] and has often been encountered experimentally.[2] In the S_N2' reaction of $Pd(PR_3)_2$ with allylic thioethers,[12] the rate decreased greatly on increasing the degree of γ-substitution, while under the present syn addition conditions the degree of γ-substitution affected the reaction rate in an irregular fashion[23] (see Table IV). Moreover, the reactivity pattern in the β- and γ-substituted substrates under syn addition conditions

(17) Fiaud, J. C.; Aribi-Zouioueche, L. *J. Chem. Soc., Chem. Commun.* **1986**, 390–392.

(18) Del Valle, L.; Stille, J. K.; Hegedus, L. S. *J. Org. Chem.* **1990**, *55*, 3019–3023.

(19) It was proposed[1d,3c,11,20] that the oxidative addition of allylic electrophiles to Ir(I), Pt(0), and Cu(I) complexes proceeds via initial complexation of the C=C bond with the metal.

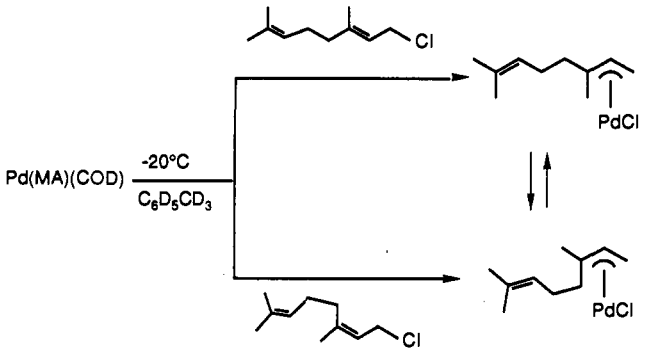
(20) Hill, R. S.; Becalska, A.; Chiem, N. *Organometallics* **1991**, *10*, 2104–2109.

(21) (a) Itoh, K. *Fundamental Research in Organometallic Chemistry*; Tsutsui, M., Ishii, Y., Yaozeng, H., Eds.; Van Nostrand: New York, 1982; p 149. (b) Howard, J. K. A.; Mitrprachachon, P.; Roy, A. *J. Organomet. Chem.* **1982**, *235*, 375–381. (c) Cheticuti, M. J.; Herbert, J. A.; Howard, J. A. K.; Preffer, M.; Spencer, J. L.; Stone, F. G. A.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1981**, 284–291. (d) Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 3801–3812. (e) Harrison, N. C.; Murray, M.; Spencer, J. L.; Stone, F. G. A. *J. Chem. Soc., Dalton Trans.* **1978**, 1337–1342. (f) Chicote, M. T.; Green, M.; Spencer, J. L.; Stone, F. G. A.; Vicente, J. *J. Organomet. Chem.* **1977**, *137*, C8–C10. (g) Rosch, N.; Hoffmann, R. *Inorg. Chem.* **1974**, *13*, 2656–2666.

(22) (a) A reviewer suggested that a less electron-rich Pd(0) complex would give a too weak complex with the substrate C=C bond to eliminate the Cl^- ion in the anti manner, so that the S_N2' path could compete with the coordination–elimination sequence, with the C–Cl bond cleavage having a partial S_N1 character (enhanced by both α- and γ-substitution). (b) Burgess, E. W.; Liotta, C. L. *J. Org. Chem.* **1981**, *46*, 1703–1708. (c) Carrion, F.; Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 3531–3539.

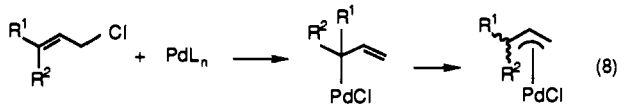
(23) The irregularity may have arisen from the two opposing effects of increasing the γ-substitution, namely, increasing steric constraint upon the C=C bond coordination and increasing intrinsic reactivity with respect to both S_N2 and S_N1 steps. It is also possible that the two methyl groups at the γ-position push the palladium atom toward the β-carbon atom when the metal coordinates with the C=C bond, so that the distance from Pd to Cl is closer in the case of the coordination of the γ,γ-dimethyl substrate than in the coordination of the γ-monomethyl substrate.

Scheme III



is much the same as that under anti addition conditions (Table IV). This is more consistent with the occurrence of C=C bond coordination also in the former case than with its absence.

As the C=C bond geometry of γ-substituted allylic substrates might be lost via a discrete η^1-allylic intermediate (eq 8),[24] it seemed of interest to examine whether this stereochemistry is retained or not in oxidative addition. We observed that under



(8)

conditions favoring syn oxidative addition (toluene-d_8, Pd(COD)(MA)), the geometry about the C=C bond of geranyl and neryl chlorides was completely retained in the initial η^3-allylic product obtained at −40 or −20 °C (Scheme III). During prolonged reaction periods, each of the two isomeric η^3-allylic complexes underwent isomerization to the other to give a ca. 1:1 equilibrium mixture[25] (compare, e.g., the half-life of η^3-geranyl formation, 25 min ([geranyl chloride] = 0.47 mol/L), with that of its isomerization to the η^3-neryl complex, 700 min at −20 °C).

In the reaction of Pd(COD)(MA) with (*Z*)-hex-2-enyl chloride in CD_2Cl_2, however, we observed the formation of no anti isomer of the (η^3-1-propylallyl)palladium chloride dimer even at −40 °C and the formation of its syn isomer only by ^{1}H NMR spectroscopy. It is possible that the anti isomer is the kinetic product in this reaction, but is too unstable to survive under the reaction conditions.[26] Or one could alternatively conceive that the reactions of the γ-substituted allylic chlorides gave η^1-allylic intermediates which retained the original C=C bond geometry about the C_α–C_β single bond, but the intermediates from neryl and geranyl chlorides possessed higher barriers to rotation about such a single bond. At the moment we cannot distinguish between the two possibilities from these stereochemical examinations.

Role of Electron-Withdrawing Olefin Ligands in Catalysis. The role of the cocatalyst, maleic anhydride, in the catalytic coupling shown in eq 4 is 2-fold. One function is to direct the stereochemical course of the oxidative addition step (see Scheme III) to syn addition in benzene, CH_2Cl_2, and THF, in agreement with the stoichiometric process. The other is to make the reaction between **2a** and the tin reagents fast and clean. The origin of this role has been elucidated before as due to the acceleration of the reductive elimination of Pd(η^3-allyl)(R)(L) where L = electron-withdrawing olefins.[10,28]

Concluding Remarks

The stereochemistry of the oxidative addition of allylic halides to Pd(0) and Pt(0) complexes was found to be more diverse than has been thought before. The necessary condition for the novel syn addition was revealed to be the use of electron-withdrawing olefin complexes in nonpolar solvents. The excessive electron flow from palladium to these olefins is not favorable for the activation of certain allylic electrophiles. The usefulness of this new principle of syn addition in synthetic application was demonstrated in selected cross coupling reactions. Although the lower reactivity of olefin–Pd(0) complexes than of ordinary phosphine–Pd(0) complexes with regard to oxidative addition might cause a limitation when this principle is to be applied to other synthetic transformations, the present findings may prompt more searches for a combination of metals and ligands in complexes and leaving groups in electrophiles that is capable of accomplishing an oxidative addition exhibiting a novel stereochemical course.

Experimental Section

All manipulations employing palladium(0) and platinum(0) complexes were carried out under argon by the use of standard vacuum line techniques. Solvents were dried by standard methods and distilled prior to use. The following materials were prepared according to reported methods: **1a**-trans;[3b] $Pd_2(dba)_3$;[29] Pd(COD)(MA), $Pd(NBE)_2$(MA), and Pd(COD)(TCNE);[30] $Pd(NBE)_3$ and $Pt(NBE)_3$;[9b] $Pt(dba)_2$;[29a] and RBu_3Sn (R = Ph, vinyl).[3b] The compound **1b**-trans was prepared by treating *cis*-5-(methoxycarbonyl)-2-cyclohexenyl alcohol (2 g, 12.8 mmol) with dimethyl sulfide (1.45 g, 23 mmol) and *N*-bromosuccinimide (3.6 g, 20 mmol) in CH_2Cl_2[31] (60–65 °C, 0.1 mmHg; 60%). The compound **1c**-trans was prepared from *cis*-5-methyl-2-cyclohexenyl alcohol,[32] CCl_4, and PPh_3 in a manner similar to that for **1a**-trans (65–70 °C, 35 mmHg; 37%). **1a**-trans and **1c**-trans thus prepared were found by ^{1}H NMR spectroscopy to contain small amounts of the cis isomers (12% and 24%, respectively), but their existence turned out to cause no problem in determining the stereoselectivity of the oxidative addition (see later). The cis isomer of **1a** was prepared by treating the corresponding cis alcohol[3b] (10.0 g, 64 mmol) with SO_2Cl_2 (4.7 g, 64 mmol) in diethyl ether (70 mL) (65–70 °C, 0.5 mmHg; 59%). This product was found to contain 13% of the trans isomer.

^{1}H NMR spectra were obtained on JEOL GSX-400 and Bruker AM600 spectrometers.

Preparation of 2. To a benzene solution (5 mL) of Pd(COD)(MA) (0.10 g, 0.32 mmol) was added dropwise a benzene solution (1 mL) of **1a**-trans (0.28 g, 1.6 mmol) at room temperature. After the mixture was allowed to stand for 0.5 h, *n*-hexane (5 mL) was added, and the mixture was kept in a refrigerator overnight to give a yellow powder of isomerically pure **2a**-trans (85%); mp 112–113 °C dec. Anal. Calcd for $C_8H_{11}O_2ClPd$: C, 34.19; H, 3.95; Cl, 12.62. Found: C, 34.30; H, 3.94; Cl, 12.44. ^{1}H NMR ($CDCl_3$): δ 1.74 (ddd, *J* = 3.6, 7.5, 17.0 Hz, 2 H), 2.22 (ddd, *J* = 3.0, 6.4, 17.0 Hz, 2 H), 3.41 (tt, *J* = 6.4, 7.5 Hz, 1 H), 3.66 (s, 3 H), 5.08 (ddd, *J* = 3.0, 3.6, 6.5 Hz, 2 H), 5.49 (t, *J* = 6.5 Hz, 1 H). For the preparation of **2a**-cis, **1a**-trans was reacted with Pd(COD)(MA) in acetonitrile in a similar way, and the solvent was evaporated under vacuum. The residue was recrystallized from CH_2Cl_2/*n*-hexane; mp 139–141 °C dec. Anal. Calcd for $C_8H_{11}O_2ClPd$: C, 34.19; H, 3.95. Found: C, 33.65; H, 3.99. ^{1}H NMR ($CDCl_3$): δ 2.00–2.06 (m, 3 H), 2.26 (br m, 2 H), 3.67 (s, 3 H), 5.21 (t, *J* = 6.3 Hz, 2 H), 5.55 (t, *J* = 6.3 Hz, 1 H). The five higher field H resonances appeared in first-order patterns in C_6D_6: δ 1.36 (tt, *J* = 5.0, 12.0 Hz, 1 H), 1.69 (dt, *J* = 5.0, 17.9 Hz, 2 H), 1.93 (dd, *J* = 12.0, 17.9 Hz, 2 H).

The following complexes were prepared similarly. **2b**-trans: mp 162–163 °C dec. Anal. Calcd for $C_8H_{11}O_2BrPd$: C, 29.52; H, 3.41; Br, 24.55. Found: C, 29.32; H, 3.46; Br, 24.58. ^{1}H NMR ($CDCl_3$): δ 1.77 (bdd, *J* = 9.0, 17.0 Hz, 2 H), 2.29 (ddd, *J* = 3.3, 6.2, 17.0 Hz, 2 H), 3.50 (tt, *J* = 6.2, 9.0 Hz, 1 H), 3.66 (s, 3 H), 5.20 (m, 2 H), 5.45 (t, *J* = 5.7 Hz, 1 H). **2b**-cis: mp 168–170 °C dec. Anal. Calcd for $C_8H_{11}O_2BrPd$: C, 29.52; H, 3.41; Br, 24.55. Found: C, 29.44; H, 3.41; Br, 24.69. ^{1}H NMR (C_6D_6): δ 1.38 (tt, *J* = 5.4, 11.5 Hz, 1 H), 1.73 (ddd, *J* = 5.4, 6.6, 18 Hz, 2 H), 1.99 (dd, *J* = 11.5, 18 Hz, 2 H), 3.16 (s, 3 H), 4.55

(24) Vrieze, K. *Dynamic Nuclear Magnetic Resonance Spectroscopy*; Jackmann, L. M., Cotton, F. A., Eds.; Academic Press: New York, 1975; p 441.

(25) Akermark, B.; Vitagliano, A. *Organometallics* **1985**, *4*, 1275–1283.

(26) In this regard, it should be pointed out that in the cross coupling of (*Z*)-oct-2-enyl chloride with organozirconiums catalyzed by [Pd(η^3-1-MeC_3H_4)Cl]$_2$/maleic anhydride in THF (the syn addition condition in our case), the C=C bond geometry was retained in the coupling products, and therefore also in the oxidative addition step.[27]

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(29) (a) Moseley, K.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1974**, 169–175. (b) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253–266.

(30) Itoh, K.; Ueda, F.; Hirai, K.; Ishii, Y. *Chem. Lett.* **1977**, 877–880.

(31) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339–4342.

(32) Goering, H. L.; Nevitt, T. D.; Silversmith, E. F. *J. Am. Chem. Soc.* **1955**, *77*, 4042–4048.

(t, J = 5.9 Hz, 1 H), 4.71 (dd, J = 5.9, 6.6 Hz, 2 H). **2c**-trans: mp 104–106 °C dec. Anal. Calcd for $C_7H_{11}ClPd$: C, 35.47; H, 4.68; Cl, 14.96. Found: C, 35.42; H, 4.66; Cl, 14.55. ^1H NMR ($CDCl_3$): δ 0.77 (dd, J = 10.6, 16.0 Hz, 2 H), 0.88 (d, J = 6 Hz, 3 H), 2.09 (ddd, J = 4.0, 6.2, 16.0 Hz, 2 H), 2.98 (m, J = 6, 10.6 Hz, 1 H), 5.00 (dd, J = 4.0, 6.3 Hz, 2 H), 5.48 (t, J = 6.3 Hz, 1 H). **2c**-cis: mp 105–108 °C dec. Anal. Calcd for $C_7H_{11}ClPd$: C, 35.47; H, 4.68; Cl, 14.96. Found: C, 35.40; H, 4.68; Cl, 14.91. ^1H NMR ($CDCl_3$): δ 0.89 (d, J = 6 Hz, 3 H), 1.15 (m, 1 H), 1.48 (dd, J = 11.7, 18.7 Hz, 2 H), 2.01 (ddd, J = 4.4, 7.3, 18.7 Hz, 2 H), 5.21 (dd, J = 5.3, 7.3 Hz, 2 H), 5.52 (t, J = 5.3 Hz, 1 H).

Preparation of 4. To an acetone/CH_2Cl_2 (3:1) solution (10 mL) of **2a**-trans (0.056 g, 0.20 mmol) was added dropwise a CH_2Cl_2 solution (0.5 mL) of PPh_3 (0.105 g, 0.40 mmol) at 0 °C. To the mixture was added a MeOH solution (0.5 mL) of NH_4PF_6 (0.064 g, 0.40 mmol) in one portion. The solvents were evaporated under vacuum. The remaining solids were extracted with CH_2Cl_2 (10 mL). To this extract was added *n*-hexane (10 mL), and the mixture was kept in a refrigerator to give a pale-yellow crystalline solid of **4a**-trans (70%); mp 185–188 °C dec. Anal. Calcd for $C_{44}H_{41}O_2F_6P_3Pd$: C, 57.75; H, 4.52. Found: C, 57.46; H, 4.64. ^1H NMR ($CDCl_3$): δ 1.22 (m, J = 5, 17 Hz, 2 H), 1.71 (br d, J = 17 Hz, 2 H), 2.68 (tt, J = 5.6, 9 Hz, 1 H), 3.59 (s, 3 H), 5.05 (br, 2 H), 6.12 (t, J = 7 Hz, 1 H). Attempts to isolate the cis analog led to a mixture of **4a**-cis and **4a**-trans (ca. 2.2:1–1:1). ^1H NMR ($CDCl_3$): δ 1.18 (m, 2 H), 1.85–1.95 (m, 3 H), 3.58 (s, 3 H), 5.10 (t, J = 6.5 Hz, 2 H), 6.32 (t, J = 6.5 Hz, 1 H). In both **4a**-trans and **4a**-cis, the P–Ph ortho protons resonated at δ 7.25 (dd, J = 9, 12 Hz), the irradiation of which resulted in an increase in the peak at δ 2.68 (ca. 20%) of the trans isomer but not those at δ 1.85–1.95 of the cis isomer.

Similarly prepared were **4b**-trans (isomerically pure) and **4b**-cis (contaminated by comparable amounts of the trans isomer). **4b**-trans: mp 190–193 °C dec. Anal. Calcd for $C_{43}H_{41}F_6P_3Pd$: C, 59.29; H, 4.74. Found: C, 59.10; H, 4.83. ^1H NMR ($CDCl_3$): δ 0.58 (d, J = 6 Hz, 3 H), 0.93 (br, 2 H), 1.06 (quint, J = 14 Hz, 2 H), 1.89 (m, 1 H), 5.05 (br, 2 H), 6.13 (t, J = 7 Hz, 1 H). ^1H NMR ($CDCl_3$) of **4b**-cis: δ 0.61 (d, J = 6 Hz, 3 H), 0.65 (m, 3 H), 1.68 (m, 2 H), 5.15 (br, 2 H), 6.18 (t, J = 7 Hz, 1 H). In both **4b**-trans and **4b**-cis, the P–Ph ortho protons resonated at δ 7.24 (dd, J = 9, 12.5 Hz). Irradiating this peak led to an increase in the resonance at δ 1.89 (ca. 15%) of the trans isomer but no increase in the resonances at δ 0.65 of the cis isomer.

Preparation of 5. To a CH_2Cl_2 solution (5 mL) of $Pt(NBE)_3$ (0.12 g, 0.25 mmol) was added **1a**-trans (0.14 g, 0.8 mmol) at room temperature. After the mixture was allowed to stand for 3 h, the solvent was concentrated to ca. 1 mL volume, and *n*-hexane was added to cause precipitation of a pale-yellow solid of **5**-cis (63%); mp 127–130 °C dec. Anal. Calcd for $C_8H_{11}O_2ClPt$: C, 25.99; H, 3.00; Cl, 9.58. Found: C, 26.40; H, 3.06; Cl, 10.08. ^1H NMR ($CDCl_3$): δ 1.87–1.99 (m, 3 H), 2.25 (dt, J = 16.5, 5.5 Hz, 2 H), 3.69 (s, 3 H), 4.94 (br, 3 H). Similar reactions using a 1:5 mixture of $Pt(dba)_2$ and maleic anhydride gave the same complex enriched in the trans isomer (80% isomeric purity). ^1H NMR ($CDCl_3$) of **5**-trans: δ 1.54 (br m, 2 H), 2.12 (ddd, J = 3.5, 6.2, 15.2 Hz, 2 H), 3.27 (br, 1 H), 3.66 (s, 3 H), 4.72 (vbr, 2 H), 4.84 (t, J = 5.2 Hz, 1 H).

Reaction of $Pd(PPh_3)_4$ with 1a-trans. To a benzene solution (1 mL) of $Pd(PPh_3)_4$ (0.12 g, 0.10 mmol) was added **1a**-trans (0.10 g, 0.57 mmol) at room temperature to cause an immediate color change from red to yellow. *n*-Hexane (10 mL) was added to cause precipitation of a yellow solid. The solid was separated by decantation, washed with *n*-hexane, and dried under vacuum. The formation of **3**-cis in the above reaction was confirmed by comparing the ^1H NMR spectra of the product with those of the complex generated by mixing **2a**-cis and 1 equiv of PPh_3 in $CDCl_3$: δ 1.61 (ddd, J = 7.5, 10.8, 17 Hz, 1 H), 1.94 (m, 1 H), 1.99 (tt, J = 5.5, 10.8 Hz, 1 H), 2.37 (dt, J = 11, 17 Hz, 1 H), 2.63 (dq, J = 6, 17 Hz, 1 H), 3.63 (s, 3 H), 4.12 (br, 1 H), 5.71 (dd, J = 6, 6.5 Hz, 1 H), 5.83 (q, J = 6.5 Hz, 1 H). The ^1H NMR spectral data for the trans isomer **3**-trans were obtained similarly by mixing **2**-trans and PPh_3: δ 1.50 (br d, J = 16 Hz, 1 H), 1.62 (m, 1 H), 2.14 (br m, 1 H), 2.60 (m, 1 H), 3.21 (tt, J = 6.8, 8.3 Hz, 1 H), 3.67 (s, 3 H), 4.11 (br, 1 H), 5.63 (t, J = 7 Hz, 1 H), 5.68 (br, 1 H).

General Procedure for Determination of Stereoselectivity in Oxidative Addition. Most of the experiments to determine the stereoselectivity of oxidative addition were performed in NMR tubes by dissolving the complex (ca. 0.016 mmol) and the substrate halides (0.080 mmol) in appropriate deuterated solvents (0.5 mL) at room temperature, except for runs employing $Pd(NBE)_3$ whose solution was prepared at −50 °C to prevent its thermolytic decomposition. In the reactions of trans isomers of the substrates contaminated by small amounts of the cis isomers, the amounts of the η^3-allyl complexes produced (almost quantitative yields) were almost identical with those of the trans substrates consumed, and the cis substrates remained nearly unreacted. Therefore, relative amounts of the two isomeric products measured were interpreted as the stereoselectivity of the reactions of the trans substrates.

In the reactions of the cis-rich substrate **1a**-cis, the ratio of [**1a**]/[complex] added was set in the range of 1–2 so that a considerable amount of the less reactive cis substrate had been consumed after the complete consumption of the Pd(0) complexes. The stereoselectivity of the reaction of the cis substrate was calculated by taking into account the amounts of each substrate consumed and each isomeric complex produced together with the selectivity of the reaction of the trans substrate as measured above.

For the reaction of in situ generated olefin–Pd(0) complexes, a CD_2Cl_2 solution (0.1 mL) of $PhBu_3Sn$ (0.009 mmol) was added dropwise to a CD_2Cl_2 solution (0.5 mL) of $Pd(\eta^3\text{-}C_3H_5)Cl$ (0.01 mmol), the appropriate olefin (0.05 mmol), and **1a**-trans (0.02 mmol) in an NMR tube at room temperature. After 2 h the solution was examined by ^1H NMR spectroscopy.

Relative Reactivity of Some Allylic Chlorides. In a typical run, a mixture of allyl chloride (0.48 mmol) and 2-methylallyl chloride (0.48 mmol) in CH_2Cl_2 (0.9 mL) was added to Pd(COD)(MA) (0.015 g, 0.048 mmol) in the same solvent (0.9 mL) at room temperature. After the mixture was allowed to stand for 1 h, the solvent and the substrates were completely evaporated under vacuum. The remaining yellow solid was dissolved in $CDCl_3$ and ^1H NMR spectra taken to determine the relative amounts of the two η^3-allylic complexes. The same procedure was followed for the reactions of $Pd(NBE)_3$ except for dissolving the complex and adding the substrate mixture at −50 °C, followed by gentle warming to room temperature.

Formation and Isomerization of η^3-Geranyl- and η^3-Nerylpalladium Complexes. In a typical run, to a toluene-d_8 solution (0.7 mL) of Pd(COD)(MA) (5.5 mg, 0.018 mmol) in an NMR tube cooled to −80 °C was added geranyl chloride (57 mg, 0.33 mmol). The tube was inserted into the NMR probe precooled to −80 °C. After ^1H NMR confirmation that no reaction had occurred, the probe temperature was raised to −40 °C, and the progress of the reaction was monitored by observing the increase in the peaks at δ 2.75 of the η^3-geranyl complex. Only the η^3-geranyl complex formed in ca. 70% yield after 4 h. Similarly, neryl chloride and Pd(COD)(MA) afforded only the η^3-neryl complex (δ 2.70) (nearly quantitative after 24 h). Raising the temperature of these solutions to −20 °C led to isomerization to give a mixture of η^3-geranyl/-η^3-neryl (1.1:1) complexes (half-life, 700 min). The initial half-life of the oxidative addition of geranyl chloride to Pd(COD)(MA) at −20 °C was ca. 25 min.

Catalytic Cross Coupling. In a typical run, to a benzene solution (2 mL) of **1a**-trans (0.4 mmol), $Pd(\eta^3\text{-}CH_2CHCH_2)Cl$ (0.02 mmol), and maleic anhydride (0.08 mmol) was added $PhBu_3Sn$ (0.4 mmol) in benzene (1 mL) at room temperature. After the reaction mixture was allowed to stand for 48 h, the solvents were evaporated under vacuum. The residue was treated with aqueous KF and diethyl ether in a manner similar to that reported before[3b] to give 3-phenyl-5-(methoxycarbonyl)-cyclohexene (60%; trans/cis = 98:2). ^1H NMR measurement of the above reaction mixture in C_6D_6 after the same reaction period showed the formation of **6**-trans in 80% yield, all **1a**-cis initially added having remained unreacted.

In the reaction of **1a**-cis (0.084 mmol) with $PhBu_3Sn$ (0.084 mmol) and 5 mol % $Pd(\eta^3\text{-}CH_2CHCH_2)Cl$/20 mol % maleic anhydride in C_6D_6 (0.5 mL), ^1H NMR measurement after 48 h showed that 0.033 mmol of **1a**-cis and 0.011 mmol of **1a**-trans reacted to give 0.023 mmol of **6**-cis and 0.021 mmol of **6**-trans. Assuming that 0.011 mmol of **1a**-trans afforded 0.010 mmol of **6**-trans and 0.001 mmol of **6**-cis, we obtain the relative amount of the product from **1a**-cis as **6**-cis/**6**-trans = 0.022:0.011 (=67:33). The other results in Table V were obtained similarly.

X-ray Structure Determination of 3-trans. A thin-plate crystal (from $CHCl_3$/*n*-hexane) with approximate dimensions of 0.05 × 0.50 × 0.70 mm was mounted on Rigaku automated four-circle diffractometer. Crystal data: $C_{26}H_{26}O_2ClPPd$, fw = 543.32, monoclinic, space group $P2_1/n$, a = 12.717 (2) Å, b = 9.881 (2) Å, c = 19.772 (3) Å, β = 105.38 (2)°, V = 2395.7 (6) Å^3, Z = 4, F(000) = 1104, D_c = 1.507 g cm^{-3}, μ(Mo Kα) = 9.60 mm^{-1}. Accurate unit-cell dimensions were determined by a least-squares fit of 2θ values of 24 reflections. Integrated intensities were collected by the θ–2θ scan technique using graphite-monochromatized Mo Kα radiation (λ = 0.71069 Å). The scan speed and width were 4 deg min^{-1} in 2θ and $\Delta 2\theta = (2.2 + 0.70 \tan\theta)°$, respectively. Background intensities were measured for 5 s at both ends of a scan. Four standard reflections measured at regular intervals showed no significant decay throughout data collection. Lp and absorption corrections were applied to the intensity data. A total of 5234 independent reflections were obtained within 2θ up to 54.0° (sin θ/λ = 0.639 Å^{-1}). The discrepancy factor for symmetry equivalent reflections ($R_{int} = \sum||F| - \langle|F|\rangle|/\sum\langle|F|\rangle$; $\langle|F|\rangle$ = the average value of two or more equivalent reflections) was 0.015.

The structure was solved by the heavy atom method and refined by the block-diagonal least-squares procedure (HBLS-V),[33] the function minimized being $\sum w(|F_o| - |F_c|)^2$. Non-H atoms were refined anisotropically, whereas all H atoms located by stereochemical considerations were refined isotropically. The weighting scheme used is $w = (\sigma_{cs}^2 + a|F_o| + b|F_o|^2)^{-1}$, where σ_{cs} is the standard deviation obtained from the counting statistics, and a and b were 0.0400 and 0.001 in the final refinement cycles. The final R and R_w values, where $R = \sum||F_o| - |F_c||/\sum|F_o|$ and $R_w = \{\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2\}^{1/2}$, are 0.043 and 0.049 for 4150 observed reflections ($|F_o| > 3\sigma(|F_o|)$). The atomic scattering factors were taken from *International Tables for X-ray Crystallography*.[34] Tables of final atomic positional parameters with B_{eq} values[35] and anisotropic temperature factors for non-H atoms, atomic parameters for H atoms, all the bond lengths and angles, and observed and calculated structure factors are available as supplementary materials (Tables S1-S5).

All computations were carried out on an ACOS 930 computer at the Research Center for Protein Engineering, Institute for Protein Research, Osaka University.

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Supplementary Material Available: Crystallographic information for **3**-trans including the atom numbering scheme (Figure S1), atomic coordinates and B_{eq} values of non-H atoms (Table S1), anisotropic temperature factors for non-H atoms (Table S2), atomic parameters of H atoms (Table S3), and bond distances and bond angles (Table S4) (6 pages); observed and calculated structure factors for **3**-trans (Table S5) (11 pages). Ordering information is given on any current masthead page.

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Cyclization Reactions of Molybdenum and Chromium Carbene Complexes with 1,6- and 1,7-Enynes: Effect of Tether Length and Composition

Daniel F. Harvey,* Kevin P. Lund, and David A. Neil

Contribution from the Department of Chemistry (0506) University of California at San Diego, La Jolla, California 92093-0506. *Received May 26, 1992*

Abstract: It has been observed that the reaction of 1,6- and 1,7-enynes with pentacarbonyl(butylmethoxycarbene)molybdenum(0) (**18**) produces vinylcyclopropanes in good to excellent yield. A systematic investigation into the factors which govern the success of these cyclizations has been performed. Chromium carbene complexes also lead to the formation of vinylcyclopropanes but in significantly lower yields. When the pathway to vinylcyclopropanes is not followed, a number of other distinct types of products are obtained. The pathways leading to these various products are discussed and compared.

Recently we reported several studies concerning the reactivity of molybdenum carbene complexes.[1,2] Of particular interest has been the ability of these complexes to react with α,ω-enynes to smoothly produce vinylcyclopropanes.[2] Due to our continuing interest in the development of Fischer carbene complex-mediated cyclization strategies for the production of polycyclic ring systems, we have investigated the impact of a variety of olefin substituents on the outcome of this reaction. Herein we report that the reaction pathway followed is highly dependent upon the metal employed as well as the nature of the functionality present on the enyne substrate.

Several groups have recently investigated the reactivity of 1,6- and 1,7-enynes with group VI Fischer carbene complexes. A number of distinct reaction pathways have been described and are shown in Scheme I. Katz and Sivavec have demonstrated that treatment of biphenyl derivative **1** with stoichiometric amounts of tungsten complex **2** gives phenanthrene derivative **3**.[3] This process is believed to occur via the intermediacy of vinylcarbene complex **4** which undergoes an olefin metathesis process with the pendant alkene via metallacyclobutane **5** to give **3** and the unstabilized tungsten carbene complex **6**. In contrast, Wulff and Kaesler have found that alternative reaction pathways are taken when unsubstituted enyne **7** is treated with chromium complex **8**.[4] When performed in acetonitrile, the major product is cyclobutanone **9**, which is suggested to arise via intramolecular 2 + 2 cycloaddition of vinylketene intermediate **12**. In tetrahydrofuran, an additional product, methoxyfuran **10**, is obtained via metal-mediated rearrangement of vinylketene **12**.[5] More recently, Korkowski, Hoye, and Rydberg have demonstrated that vinylcyclopropane formation is the dominant pathway when substituted enyne **13** is treated with chromium carbene complex **8**.[6] This presumably occurs via intramolecular cyclopropanation of the pendant alkene by vinylcarbene complex **15**. In addition, Hoye and co-workers have noted that enynes related to **13**, but with additional substitution on the olefin, give rise to cyclobutanones and/or furans related to **9** and **10** as well as to olefin

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