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PALLADIUM CATALYZED COUPLING REACTIONS: MECHANISM OF REDUCTIVE ELIMINATION

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ABSTRACT

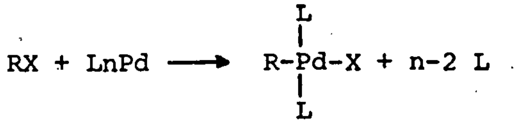
The 1,1-reductive elimination of ethane from three cis-bis(phosphine)-dimethylpalladium complexes, $L_2Pd(CH_3)_2$ ($L=PPh_3, PPh_2CH_3$ and $L_2=Ph_2PCH_2CH_2PPh_2$), and three trans analogs [$L=PPh_3$, PPh_2CH_3 and L_2=2,11-bis(diphenylphosphinomethyl)benzo(c)phenanthrene (TRANSPHOS)] was carried out. The three cis complexes underwent reductive elimination in the presence of coordinating solvents (DMSO, DMF, and THF). The trans complexes which could isomerize to cis ($L=PPh_3$, PPh_2CH_3) did so in polar solvents and then underwent reductive elimination. TRANSPHOS dimethylpalladium would not undergo reductive elimination of ethane. The eliminations from the cis isomers were intramolecular and displayed first order kinetics. Although TRANSPHOS dimethylpalladium(II) would not undergo a 1,1-reductive elimination of ethane, the addition of CD_3I to a DMSO solution of this complex at 25°C rapidly produced CD_3-CH_3, implicating a transient palladium(IV) intermediate.

E- and Z-bromostyrylbis(diphenylmethylphosphine)palladium(0) react with methyl lithium in THF at ambient temperature to give the E- and Z-propenylbenzenes, respectively. At -78°C, the intermediate E- and Z-styrylmethylbis(diphenylmethylphosphine)palladium(II) complexes (**9a,b**) can be isolated. On raising the temperature of solutions of **9a,b** in THF, E- and Z-propenylbenzenes are produced. The reductive elimination reaction is intramolecular and first order in dialkylpalladium(II) complex.

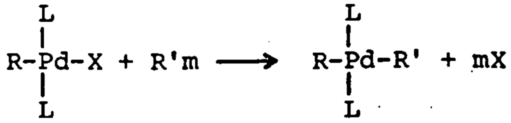
PALLADIUM CATALYZED COUPLING REACTIONS: MECHANISMS OF REDUCTIVE ELIMINATION

The coupling reaction of organic compounds catalyzed by transition metals is an important method of generating carbon-carbon bonds, the final step of which requires the elimination of the organic partners from the transition metal. The reductive elimination can take one or more paths, categorized according to the mechanism (and products), including heterolytic as well as homolytic or concerted α-elimination, β-elimination, 1,1-reductive elimination, and dinuclear elimination.[1-6] In the 1,1-reductive elimination reaction, the formal oxidation state and the coordination number of the metal are reduced by two; bond breaking is accompanied by bond making. The reductive elimination reaction frequently follows an oxidative addition reaction, and this combination, oxidative addition-reductive elimination is responsible for both stoichiometric and catalytic coupling reactions via transition metals, particularly those of Group VIII. Critical mechanistic studies on the 1,1-reductive elimination reactions of diorganopalladium complexes are scarce, yet palladium has been demonstrated to catalyze a large number of different coupling reactions in which reductive elimination is part of the sequence.

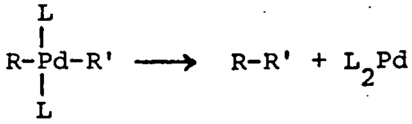
Palladium(0) catalyzed the coupling of benzyl halides with organometals, such as Grignard reagents and organolithium compounds. In a number of studies the 1,1-reductive elimination of organic partners from bis(phosphine)diorganopalladium(II) complexes has been carried out as a model for that step in the catalytic coupling reaction[7,8] (eq 1c). For example, trans-bis(phosphine)-methylphenylpalladium(II) complexes decompose thermally to give toluene.[8] One of the probelms to be examined in such a 1,1-reductive elimination reaction, therefore, is the mechanism by which the two trans organic partners eventually become coupled. In catalytic coupling reactions proceeding by



$$RX + LnPd \longrightarrow R\text{-}\overset{\displaystyle L}{\underset{\displaystyle L}{Pd}}\text{-}X + n\text{-}2\ L \qquad (1a)$$



$$R\text{-}\overset{\displaystyle L}{\underset{\displaystyle L}{Pd}}\text{-}X + R'm \longrightarrow R\text{-}\overset{\displaystyle L}{\underset{\displaystyle L}{Pd}}\text{-}R' + mX \qquad (1b)$$



$$R\text{-}\overset{\displaystyle L}{\underset{\displaystyle L}{Pd}}\text{-}R' \longrightarrow R\text{-}R' + L_2Pd \qquad (1c)$$

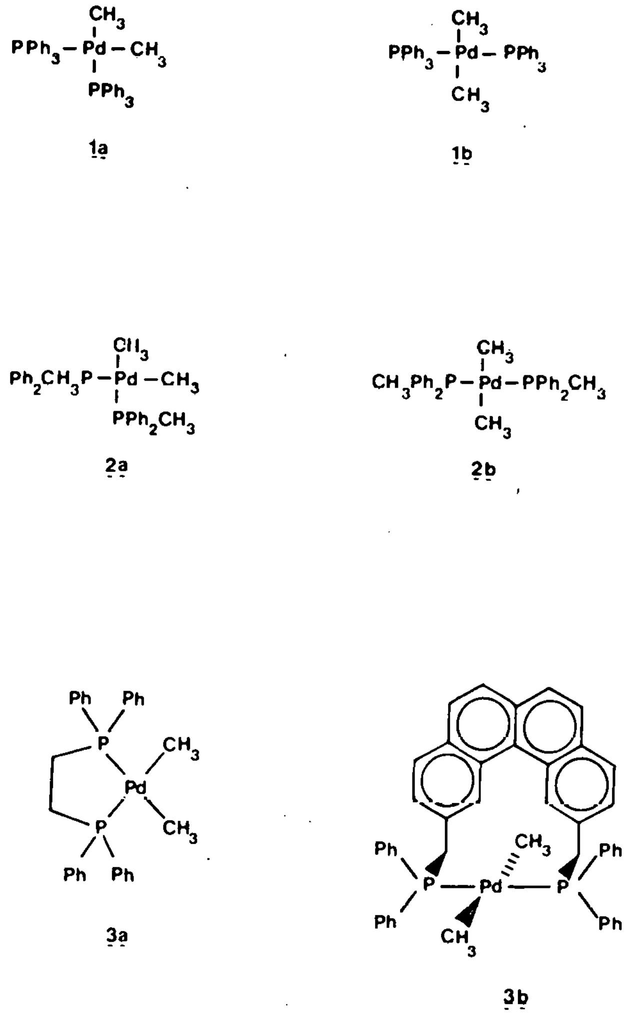
the oxidative addition-methathesis sequence, the trans complex is obtained;[8,9] however, if isomerization to the cis complex is slow compared to reductive elimination, the transient cis complex might not be observed.

In order for concerted thermal 1,1-reductive elimination to take place, it has been argued that the organic moieties must occupy adjacent positions in the complex.[2,6,10] Contruction of an orbital correlation diagram for cis four coordinate square planar d^8 complexes reveals that the concerted elimination is symmetry allowed.[11] Although the thermal concerted elimination directly from the trigonal bipyramidal and the tetrahedral complexes is symmetry allowed, 1,1-reductive elimination from a trigonal 3-coördinate species is symmetry forbidden.[10] The "T"-shaped geometry of a d^8 trimethyl gold(III) complex, however, represents a minimum energy configuration, and reductive elimination as well as cis-trans isomerization of the "T"-shaped complexes proceeds through a "Y"-shaped saddle point.[12]

There are a number of conceivable pathways by which the two organic groups in a trans complex could gain positions adjacent to one another prior to coupling: 1) Oxidative addition of an organic halide to the palladium(II) complex. 2) Prior dissociation of a phosphine to give a 3-coordinate intermediate (dissociative mechanism). 3) Prior association of a phosphine to give a 5-coordinate complex (associative mechanism). 4) Conversion of the complexes in 2 or 3 to the cis square planar complex by recoordination or dissociation of phosphine (after rearrangement), respectively. 5) Distortion of the trans complex into a transient tetrahedral geometry.

1,1-REDUCTIVE ELIMINATION OF ETHANE FROM DIMETHYL PALLADIUM

The reductive elimination reactions of dimethylpalladium complexes was studied because they have been shown to produce ethane on decomposition;[8] the β-elimination pathways is not available. Six palladium complexes (Fig 1)[13-15]



1a 1b

2a 2b

3a 3b

Figure 1. Dimethylpalladium(II) complexes.

were studied. Complex 3b was obtained by the reaction of methyl lithium with the known[16,17] trans-dichloro complex. The geometries of the structures of the dimethyl complexes were confirmed by their ^{31}P[18,19] and ^{13}C[20] spectra.

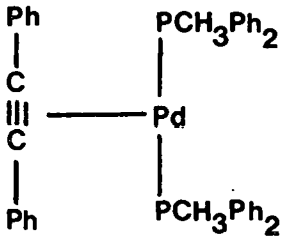
Cis-Trans Isomerization. Trans complexes 1b and 2b do not isomerize to the corresponding cis complexes in relatively non-polar solvents such as benzene or tetrachloroethane even at 100°C. No reductive elimination took place from the trans complexes. Complete trans to cis isomerization takes place only in more polar, coordinating solvents such as THF, DMF and DMSO. The position of the equilibrium between cis and trans complexes can be changed by the polarity of the medium and can be reached from either cis or trans isomer. Thus, in benzene, the position of the equilibrium depends on the amount of added polar solvent, the content of the cis isomer being higher the more polar the medium. Cis complex can be isomerized to trans complex in deuterobenzene provided a relatively non-polar coordinating species such as phosphine is present. These isomerizations are rapid at moderate temperatures ∿45°C and no evolution of ethane takes place. The 1,1-reductive elimination takes place only from the cis isomers above 45-60°C in polar solvents but not readily in non-polar solvents such as benzene. At these temperatures, no reductive elimination takes place from the trans complexes regardless of the solvent. Although the DIPHOS dimethylpalladium complex 3a underwent 1,1-reductive elimination in DMSO at 80°C, the *TRANSPHOS dimethylpalladium complex, 3b, failed to undergo reductive elimination of ethane at 80°C for 10 hours.*

These observations show that isomerization of the dimethylpalladium complexes requires the presence of a coordinating solvent or a phosphine, suggesting a five coordinate intermediate or transition state. Increasing the polarity of the solvent increases the population of the cis complex. For coupling to occur, the groups must occupy cis positions but reductive elimination takes place only in polar solvents.

Crossover Experiments. DMSO solutions containing equimolar amounts of the cis isomers 1a, 2a or 3a and their corresponding perdeuteromethyl analogs undergo reductive elimination to give only ethane and d_6-ethane. No trideuteroethane could be detected, demonstrating that no exchange of methyl takes place between complexes, and that the reductive elimination is mononuclear and intramolecular.

Kinetics. The reductive elimination reactions from the cis complexes were first order, the relative rates being 1a>2a>3a. Trans-bis(triphenylphosphine)dimethylpalladium (1b) underwent rapid and complete isomerization in d_6-DMSO at 60°C to yield the cis complex (1a) prior to the elimination of ethane. After an induction period, which corresponded to the isomerization of trans to cis, the first order kinetic plot was linear with a rate constent identical to that obtained by starting with the cis isomer (Fig 2).

The addition of excess phosphine ligand or diphenylacetylene has been reported[21] to stabilize a platinum(0) species formed as a result of reductive elimination from its hydridomethyl complex. The addition of excess diphenylmethylphosphine to a d_6-DMSO solution of 2a significantly slowed the rate of reductive elimination of ethane. The addition of an equivalent of diphenylacetylene, however, gave reaction rates which were in agreement with the rates obtained for 2a without added acetylene. The palladium acetylene complex (4) could be isolated from the reaction solution.



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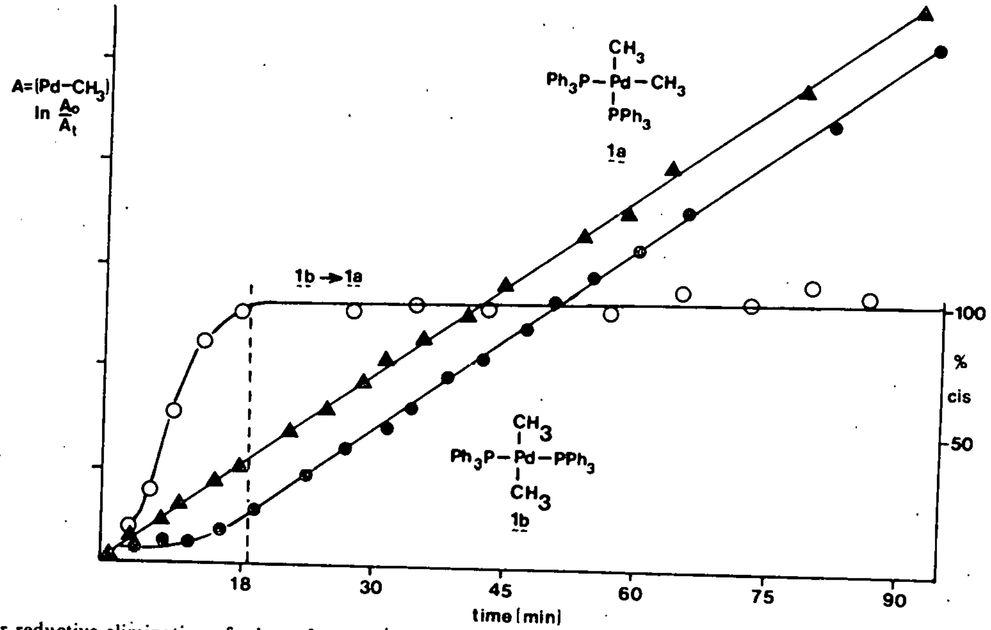


Figure 2. First-order reductive elimination of ethane from **1a**: ●, produced by isomerization of **1b**; ▲, **1a**; ○, isomerization **1b** → **1a**.

Mechanisms of Reductive Elimination. There are certain requirements for reductive elimination of ethane from bis(phosphine)dimethylpalladium(II) complexes to take place. First, only a cis complex will undergo the 1,1-reductive elimination. A polar solvent is necessary to stabilize the cis complex, and a polar, coordinating solvent is necessary for the isomerization of a trans complex to the cis complex.

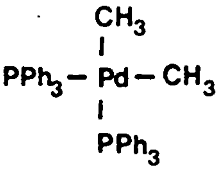
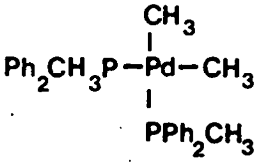
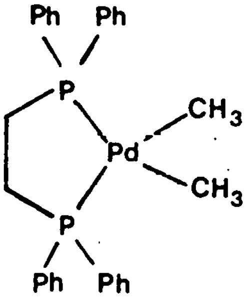
Second, polar/coordinating solvents enhance the reductive elimination.

Both the ^1H and ^{31}P NMR spectra show that initially 50% of the coordinated phosphine is displaced from complexes 1a and 2a. This dissociation does not occur in non-polar/coordinating solvents such as deuterobenzene a solvent in which the reductive elimination does not take place. The cis chelating ligands, DIPHOS, does not dissociate in the detectable amount from complex 3a, even in the presence of strongly polar/coordinating solvents.

The rates of reductive elimination for the cis complexes are 1a>2a>3a (Table I). Although reductive elimination can take place directly from cis complexes 1a-3a, this order parallels the ability of the complex to dissociate phosphine; added phosphine retards the rate of elimination (eq 2a). The cis chelating ligand, DIPHOS, does not dissociate from 3a in a detectable amount. The greater difficulty with which 3a dissociates one of the phosphines accounts for a rate of reductive elimination which is 50-100 times slower than for 2a, a complex that is electronically and geometrically similar. It is not clear, however, whether the function of the polar/coordinating solvent is to aid in phosphine dissociation by solution or by occupying the coordination site vacated by phosphine. The σ-donating ability of the phosphines, which enhances oxidative addition, thus inhibits reductive elimination. Reductive elimination may occur either from the cis squar planar complex containing coordinated solvent or from a tricoordinate Y shaped intermediate similar to that reported[12] for trimethyl gold. Once elimination has occurred (eq 2b), the dissociated ligands recoordinate to palladium(0) as evidenced by the decreasing amount of free phosphine as the reaction proceeds (eq 2c). These results and the mechanism are in direct contrast to those for the reductive elimination of biphenyl from <u>cis</u>-bis(phosphine)diphenylplatinum(II)

Table I

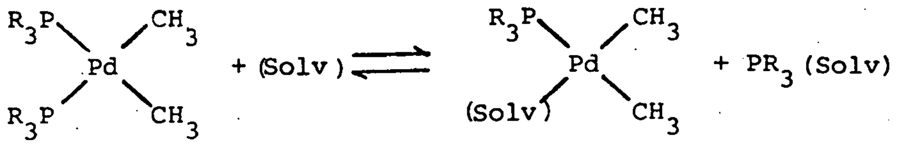
cis complex

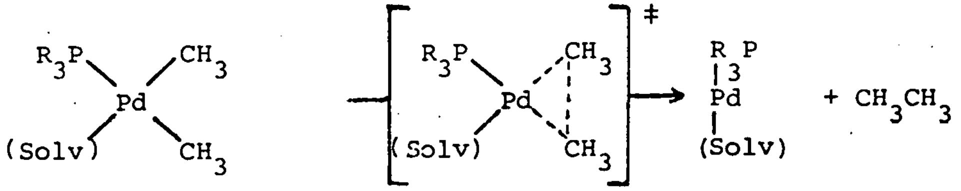
	T(°C)	k (s^{-1}) (cor. coef.)	$t_{1/2}$ (sec)
 $\mathrm{PPh_3{-}\overset{\displaystyle CH_3}{\underset{\displaystyle PPh_3}{Pd}}{-}CH_3}$ 1a	60°	1.0411×10^{-3} (0.9997)	6.61×10^{2}
 $\mathrm{Ph_2CH_3P{-}\overset{\displaystyle CH_3}{\underset{\displaystyle PPh_2CH_3}{Pd}}{-}CH_3}$	60°	6.5322×10^{-5} (0.994) [a]	1.08×10^{4}
		8.3338×10^{-5} (0.9479) [b]	
2a		9.6250×10^{-5} (0.9997) [c]	7.2×10^{3}
 3a	80°	4.778×10^{-7} (0.985)	1.45×10^{6}

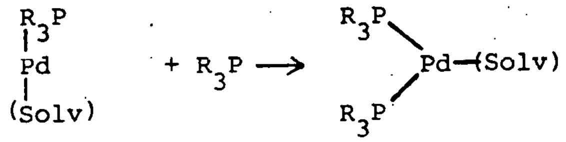
[a] With added diphenylacetylene

[b] Initial rate constant, 4

[c] Initial rate constant, 2a


(2a)

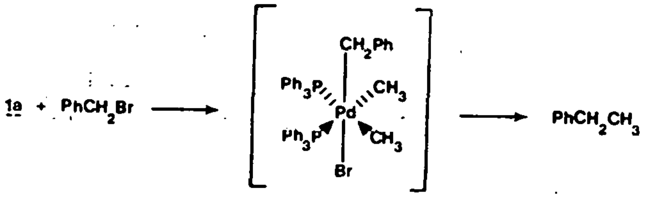

(2b)


(2c)

complexes. Because elimination is facilitated by added phosphine, the reductive elimination was proposed to proceed by a 5-coordinate intermediate or by way of a transition state involving nucleophilic attack by phosphine at palladium and simultaneous aryl-aryl bond formation.[22]

The 1,1-reductive elimination generates a palladium(0) complex which, in a catalytic coupling reaction of an organic halide with an organometal, could undergo oxidative addition of the organic halide. It has been pointed out, however, that the rates of reductive elimination are much slower than can be accommodated by a catalytic process.[23]

1,2-Bis(diphenylphosphino)ethanedimethylpalladium undergoes reductive elimination of ethane rapidly, however, upon the addition of methyliodide; the intermediate trimethyliodopalladium(IV) species being too unstable to isolate.[8] Palladium(0) catalyzed the cross coupling reaction of benzyl halides with Grignard reagents or tetraorganotin compounds.[24,25] When the reaction is carried out by first isolating the oxidative addition product of benzyl bromide to palladium(0), and then allowing the metathesis reaction to occur, in addition to coupling, other reactions take place, including α-elimination, and the rate of the reaction is much slower than when benzyl halide is present. When **1a** reacts with benzyl bromide, ethyl benzene is the only product, again supporting a transient palladium(IV) intermediate (**5**) in the reductive elimination and in the catalytic cycle.[25]



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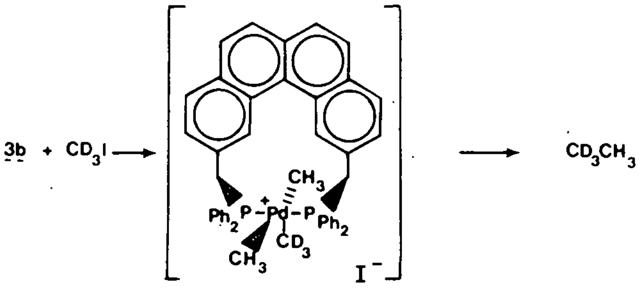
Although complex **3b**, which is held in a geometry such that the methyl groups are trans, would not undergo reductive elimination at 100°C in d_6-DMSO, the addition of methyl iodide to a solution of **3b** at room temperature immediately produced ethane. The addition of perdeuteromethyl iodide produced only 1,1,1-trideuteroethane, compelling evidence for palladium(IV) intermediate **6**.

These results on the reductive elimination from dimethylpalladium complexes have now been published in detail.[26]



6

1,1-REDUCTIVE ELIMINATION OF PROPENYLBENZENE FROM STYRYLMETHYLPALLADIUM

A study of the reductive elimination reactions of propenylbenzene from both E- and Z-styrylmethylbis(diphenylmethylphosphine)palladium(II) had the advantage that the E-,Z-geometry associated with the elimination could be observed. In addition these dialkyl palladium(II) complexes undergo cis-trans isomerization (complex geometry) and reductive elimination rapidly below ambient temperature.

Reaction Products. The oxidative addition reactions of E- and Z-β-bromostyrene with tetrakis(diphenylmethylphosphine)palladium(0) give the trans complexes (7a,b) with 100% retention of geometry at the double bond (Fig. 3). Reaction of these complexes with methyllithium at ambient temperature produced E- and Z-propenylbenzenes (8a,b) respectively, uncontaminated with the other isomer. The styrylmethylpalladium(II) complexes were too unstable to be isolated at room temperature.

Both the E- and Z-styrylmethylbis(diphenylmethylphosphine)palladium(II) complexes (9a,b) could be isolated from THF solutions by the reaction of 7a and 7b with methyllithium at -78°C. Mixtures of the cis and trans isomers of 9a and 9b were obtained. Decomposition of these E- and Z-styrylmethyl-

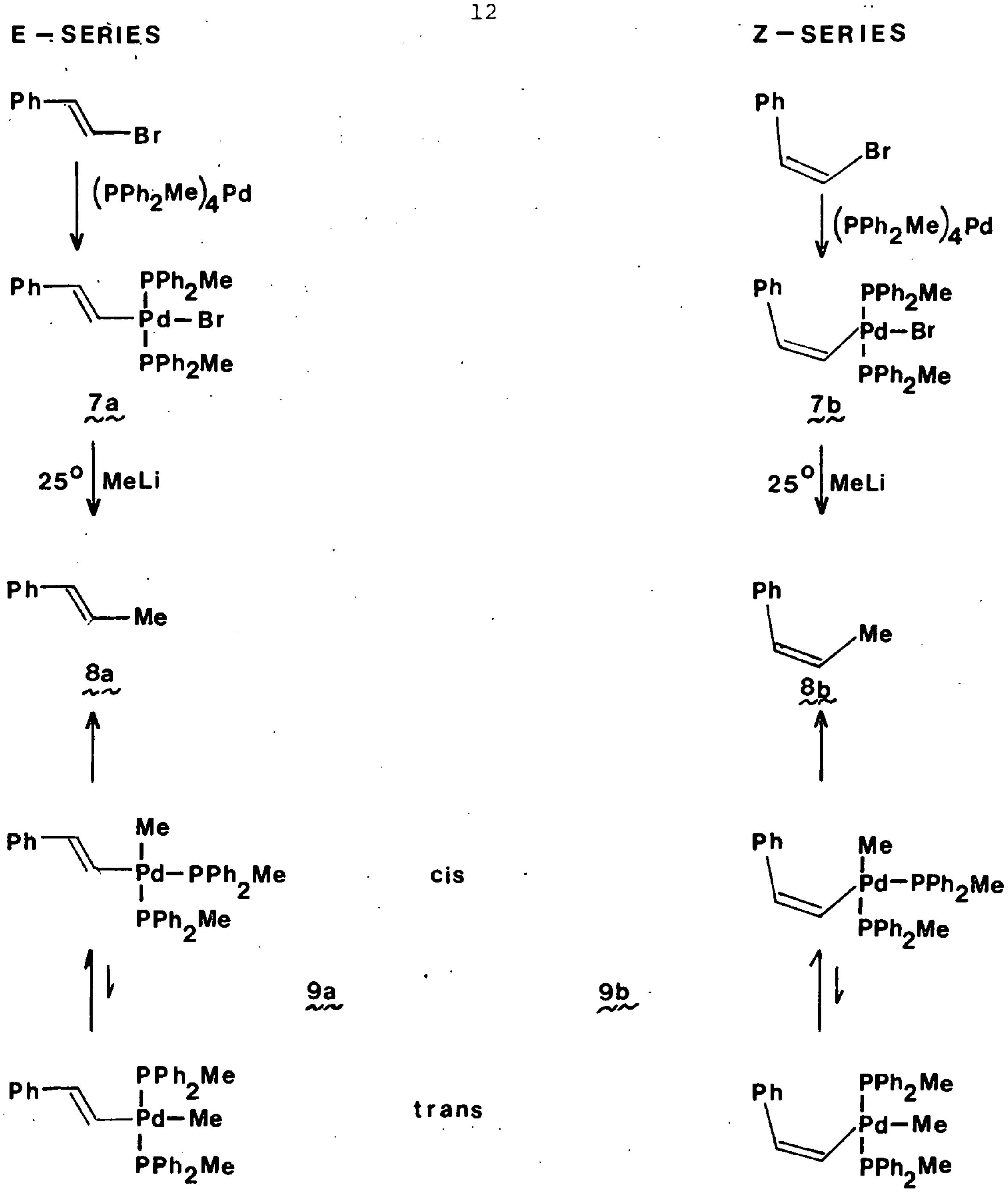


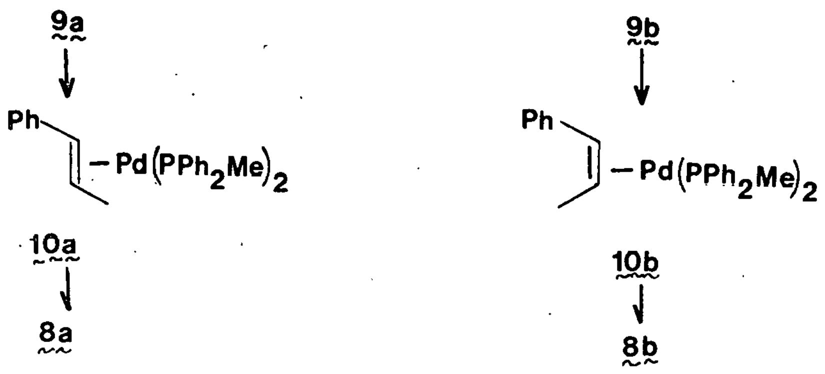
Figure 3. Cis and Trans, E- and Z- Styrylmethylbis-(diphenylmethylphosphine) Palladium(II) Elimination Reactions

palladium complexes (9a and 9b) produced the corresponding E- and Z-propenylbenzenes (8a,b) respectively.

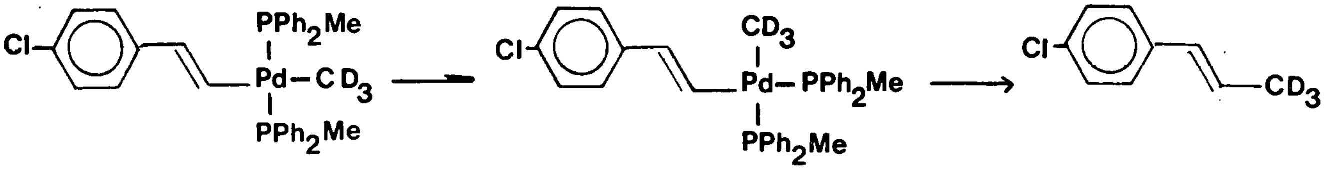
The cis-E- and Z-styrylmethylpalladium complexes underwent rapid decomposition whereas the more thermally stable trans complexes isomerized to cis geometry before reductive elimination could occur. Added diphenylmethylphosphine rapidly isomerized the trans isomers to the cis isomers either in THF or toluene.

These results show that the same requirements are necessary for reductive elimination in these complexes as are demanded by the dimethylpalladium complexes. First, the alkyl groups must occupy cis positions in the complex. The trans complex must isomerize first to place the alkyl groups in adjacent positions before reductive elimination can occur. The isomerization is catalyzed by phosphine, but the cis isomers are preferred regardless of the polarity of the solvent. In addition the elimination takes place with complete retention of geometry at the double bond.

The elimination reaction was shown by low temperature nmr to involve the intermediate π-olefin complexes, E- and Z-(propenylbenzene)bis(diphenylmethylphosphine)palladium(0) (10a,b), which lost E- and Z-propenyl benzene respectively.



Crossover Experiments. Two complexes, a cis-trans mixture of E-styrylmethylbis(diphenylmethylphosphine)palladium(II) (**9a**) and a cis-trans mixture of E-p-chlorostyryltrideuteromethylbis(diphenylmethylphosphine)-palladium(II) (**11**) were prepared. An equimolar mixture of these two complexes in THF was subjected to the 1,1-reductive elimination reaction to give only E-propenylbenzene (**8a**) and E-p-chloro-3,3,3-trideuteropropenylbenzene (**12**). No crossover products were observed. Thus, neither exchange of the methyl nor styryl groups takes place prior to reductive elimination. The elimination is intramolecular and does not take place from a dinuclear palladium complex.



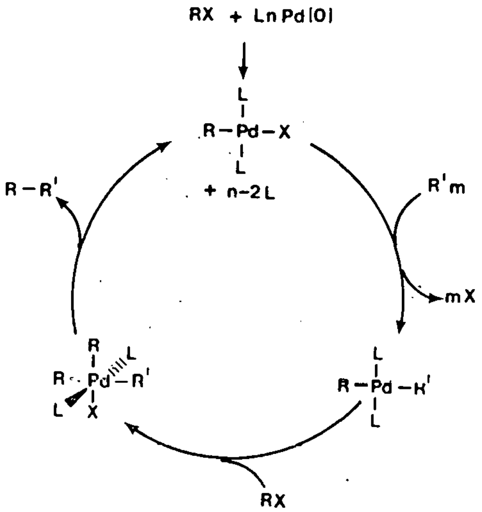
trans **11** cis **12**

Kinetics. The coupling reaction takes place by first dissociating a phosphine ligand. As a result, the coupling reaction is autocatalytic, since the intermediate product of the reductive eliminations, the olefin palladium(II) complexes (**10a** or **10b**), scavange triphenylphosphine from solution and shifts the phosphine dissociation equilibrium from the styrylmethyl palladium complexes (**9a**,**b**). In the presence of excess diphenylmethylphosphine, the reductive eliminations were first order.

When deuteromethyl iodide was added to a THF solution of cis and trans E-styrylmethylbis(diphenylmethylphosphine)palladium(II) (**9a**) at -78°C some

3,3,3-trideuteromethylpropenylbenzene was formed, implying that a palladium(IV) species can be the responsible intermediate in a reductive elimination reaction. The elimination reaction involving a palladium(IV) species obviously can take place at low temperatures.

In view of these results, the results obtained from the reaction of the dimethyl TRANSPHOS palladium complex (3b) with trideuteromethyl iodide and the knowledge that organopalladium complexes undergo reductive elimination with retention of configuration at carbon bound to palladium,[24] reductive elimination in this type of catalytic coupling reaction involved a concerted process from a palladium(IV) complex. Since the oxidative addition metathesis reaction gives a palladium(II) complex in which the organic partners are trans, then this explains how a palladium complex containing adjacent organic groups can be realized. It also explains the presence of homocoupling products, as well as cross-coupled material in many coupling reactions. The kinetics of this elimination from palladium(IV) are now being determined.



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