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MASTER

ABSTRACT

The coupling reaction of benzyl halides and organolithium, organotin or Grignard Reagents is catalyzed by palladium. The sequence of events in the catalytic cycle is oxidative addition of the benzyl halide to palladium(0), methathesis by the organometallic reagent to give a benzyl methyl palladium(II) complex, oxidative addition of the benzyl halide to give a palladium(IV) complex, and reductive elimination of benzyl and methyl to give ethylbenzene. The reductive elimination from palladium bearing an optically active α-deuteriobenzyl group takes place with retention of configuration at carbon, and is therefore concerted or nearly concerted. Since ρ is positive in the catalytic reaction with substituted aryl halides an oxidative addition, probably during the Pd(II) to Pd(IV) reaction, is the slow step in the catalytic cycle.

The intermediate diorganopalladium species can be isolated when the two groups attached to palladium are both methyl or methyl and either cis or trans-β-styryl. The decomposition of these species can be followed by nmr. In the case of methylstyrylpalladium(II) complexes, the reductive elimination gives propenyl benzene with stereospecific retention of double bond geometry. Cis-dimethylbis(diphenylmethylphosphine)palladium(II) does not undergo isomerization to the more stable trans isomer in an inert solvent, and is stable toward reductive elimination up to 50°. In the presence of added phosphine, or in a coordinating solvent, rapid cis to trans isomerization and reductive elimination to give ethane is observed. An associative mechanism is apparently operative in this case.

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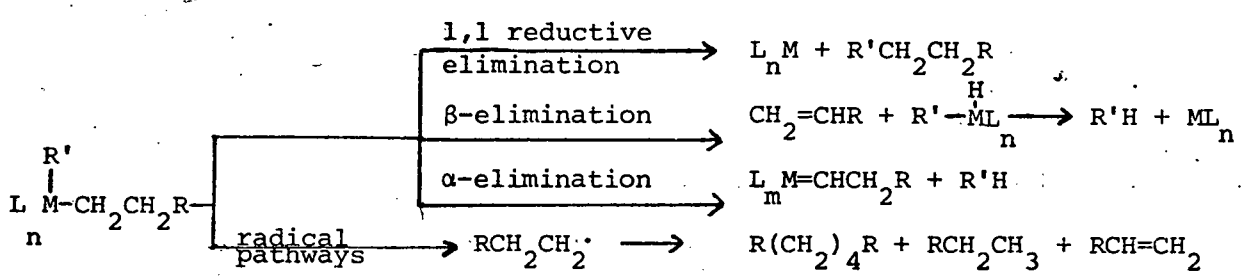
PALLADIUM CATALYZED COUPLING REACTIONS:
MECHANISM OF REDUCTIVE ELIMINATION

The coupling reaction of hydrocarbons or other organic reagents catalyzed by transition metals is one of the most important methods of generating carbon-carbon bonds, yet it is a reaction about which little mechanistic information is available. The final step in these coupling reactions is the elimination of the organic partners from the transition metal by a reductive elimination, breaking carbon-metal σ-bonds. The elimination may take one or more paths that can be categorized according to the mode of elimination and/or products.[1-3]

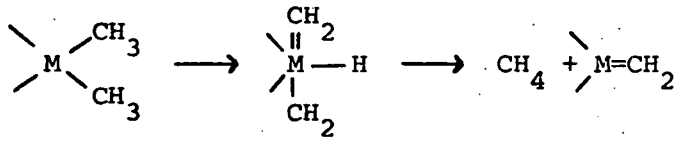


In the 1,1-reductive elimination reaction, the oxidation number and often the coordination number of the metal are reduced by two; bond breaking is accompanied by bond making. The reductive elimination reaction frequently follows an oxidative addition reaction, and this combination, oxidative addition-reductive elimination is responsible for both stoichiometric and catalytic coupling reactions via transition metals. 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 a reductive elimination reaction is a part of the sequence. Elucidation of the mechanism of reductive elimination was undertaken, in part, to define optimum conditions for this step in the catalytic cycle.

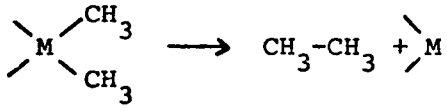
RESULTS

The basic approach to understanding the mechanism of 1,1-reductive elimination of two organic groups σ-bonded to palladium centers around the isolation or transient generation of such a complex, and its decomposition under various conditions. Complexes containing organic groups having β-hydrogens have been avoided, initially, to obviate complication posed by that decomposition pathway.

Decomposition by β-hydrogen elimination is the most frequently observed reactions, but when no β-hydrogen is available, alternate decomposition pathways are followed. However, in complexes containing two organic groups on the metal, the decomposition paths are often diverse and the mechanism are poorly understood. Certain di- or trimethyl metal complexes decompose to give methane.[4] Mechanisms involving the intermediacy of a metal carbene[5,6] have been documented in only a few cases[7] and the detection of such a species has been observed in essentially none of these cases.



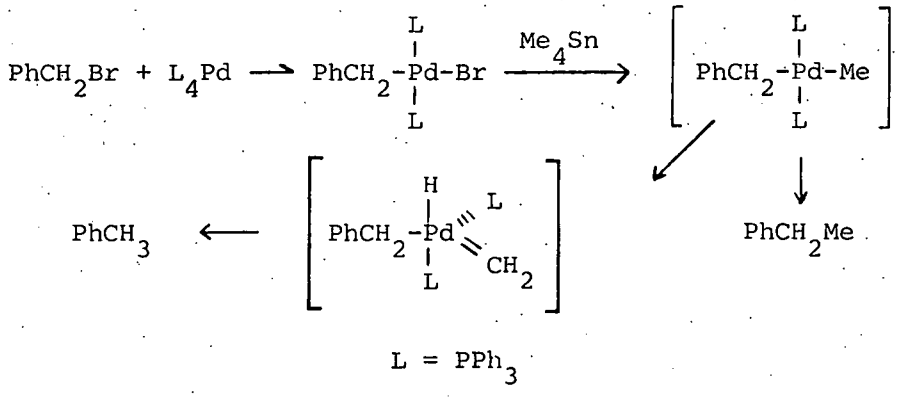
By contrast other methyl metal complexes give ethane by a concerted 1,1-reductive elimination.[8,9]



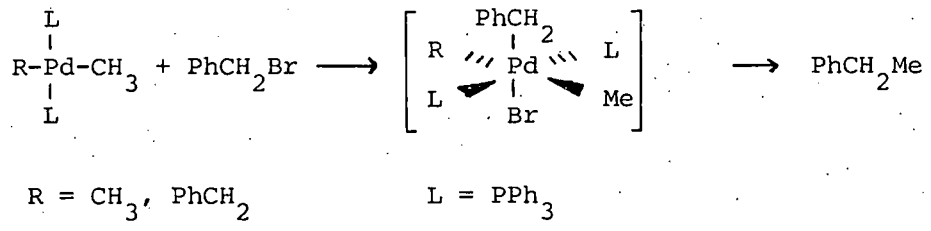
<u>Reductive Elimination of Benzyl and Methyl from Palladium</u>[10,11]

Palladium(0) complexes catalyze the coupling of benzyl halides with Grignard reagents or tetraorganotin compounds. The reaction gives only cross-coupled products provided the benzyl halide is present during the

reaction. When the coupling 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, other reactions take place, including α-elimination, and the rate of elimination is much slower than when benzyl halide is present. When cis-dimethylbis(triphenylphosphine)palladium(II)

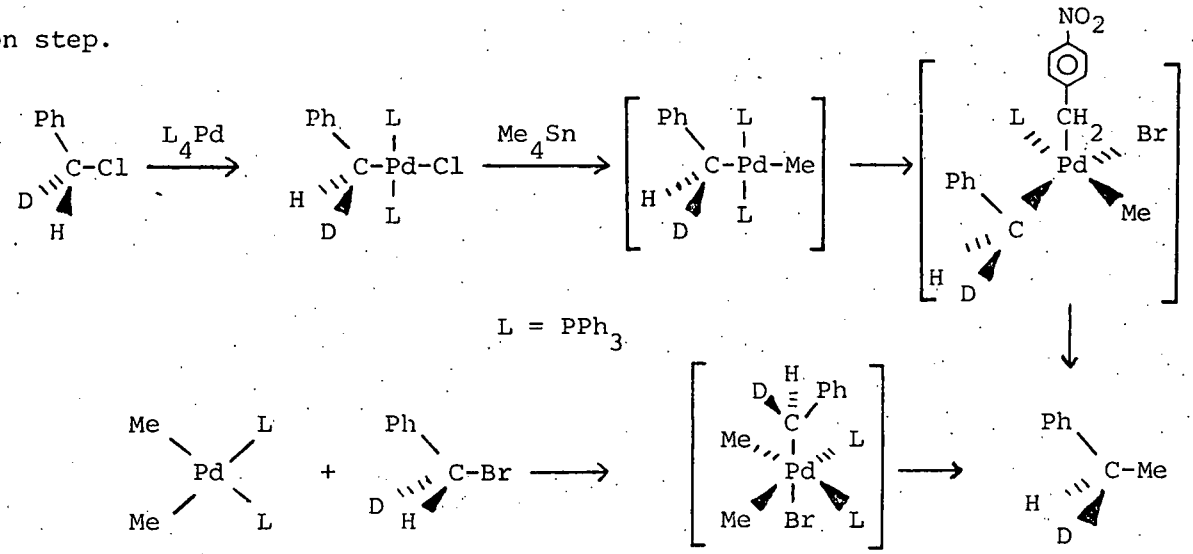


reacts with benzyl bromide, ethyl benzene is the only product. This and other evidence supports a transient Pd(IV) intermediate in the reductive elimination.

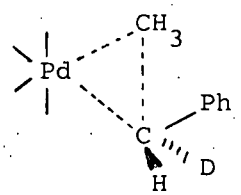


Optically active chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium yields, upon reaction with tetramethyltin (in the presence of a benzyl halide, p-nitrobenzyl bromide, for example), optically active α-deuterioethylbenzene in which retention of configuration at carbon has resulted in the reductive elimination. Further, the reaction of α-deuteriobenzyl bromide with cis-dimethylbis(triphenylphosphine)palladium(II) produces optically active α-deuterioethylbenzene with inversion of configuration at carbon taking place. Since oxidative addition to low valent

palladium species takes place with inversion of configuration at carbon,[12] then retention of configuration is taking place in the reductive elimination step.



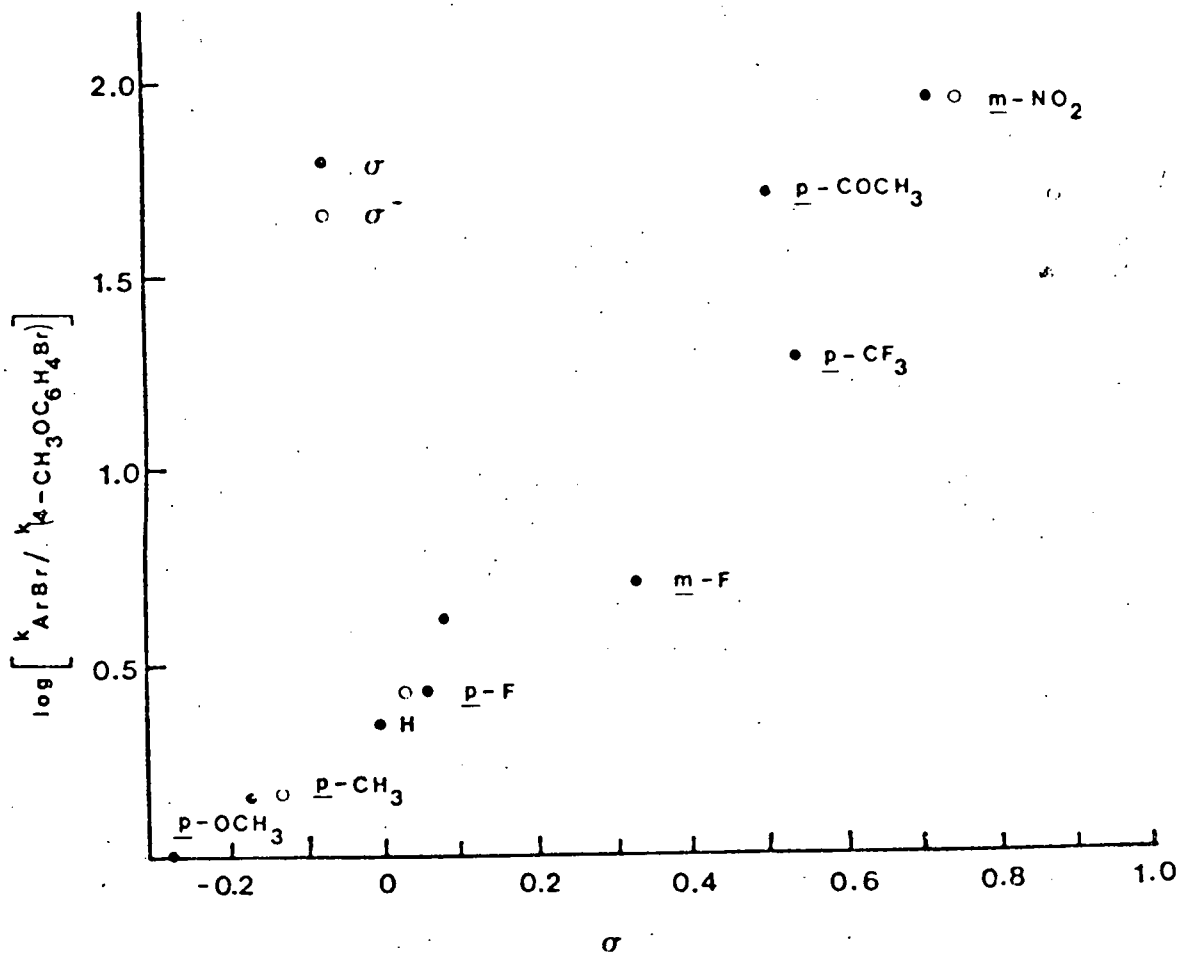
Therefore, the mechanism of bond making and breaking in the 1,1-reductive elimination is a concerted or nearly concerted process from a palladium(IV) species.



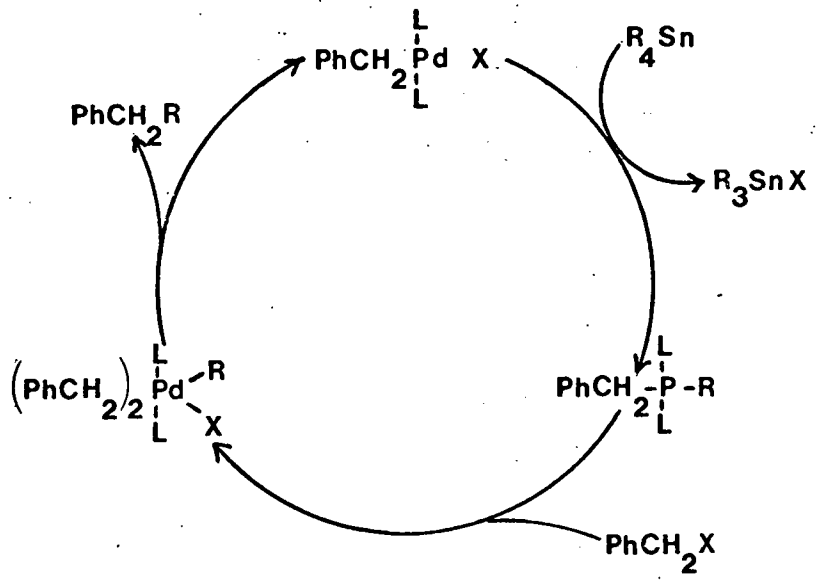
The reaction of tetraorganotin compounds with benzyl and aryl halides catalyzed by palladium is an efficient synthetic method for preparing such cross-coupled products. A variety of functional groups are tolerated by this reaction and oxygen has an accelerating effect. The reaction of substituted bromobenzene with tetramethyltin catalyzed by palladium is accelerated by electron withdrawing groups; however, a simple Hammett correlation is not observed (Fig. 1).

Fig. 1

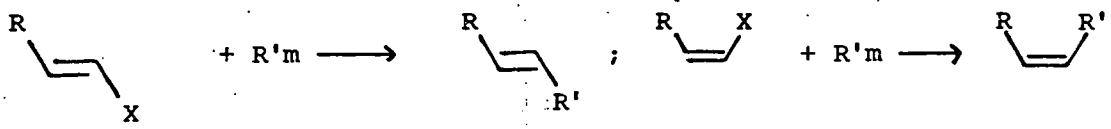
Hammett Plot of the Reaction of Substituted Bromobenzenes with Tetramethyltin



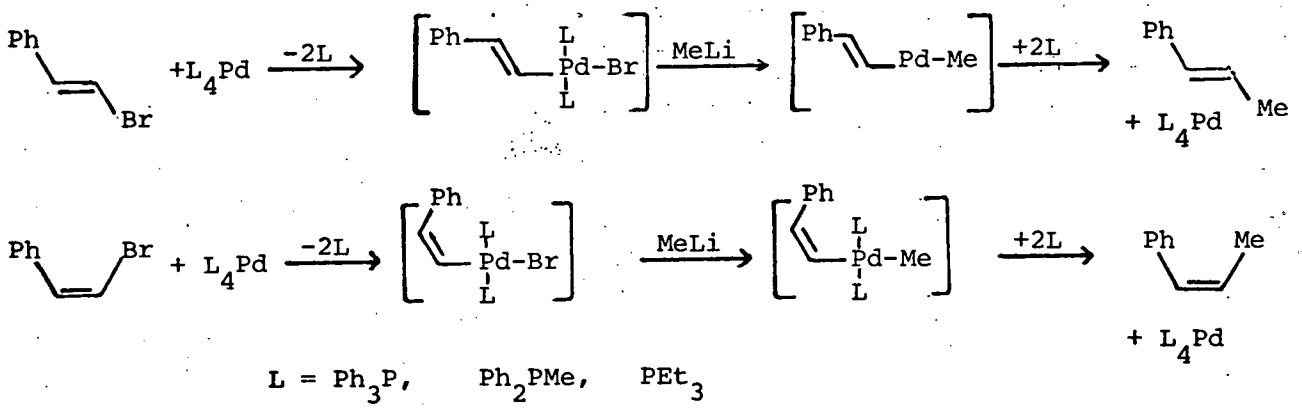
The main catalytic cycle for this reaction involves Pd(II)-Pd(IV) oxidation-reduction sequences.



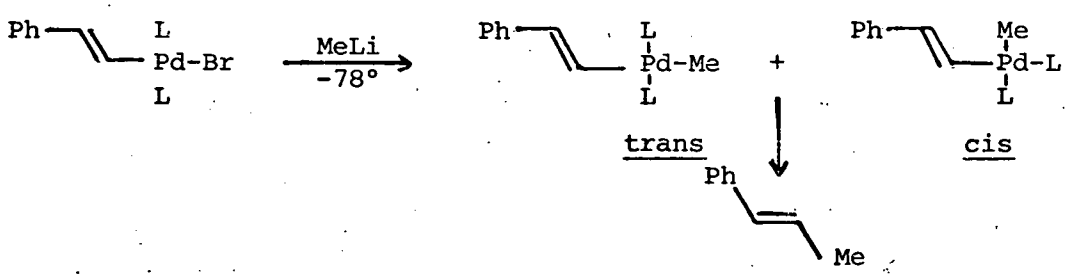
Reductive Elimination of Vinyl and Methyl from Palladium. In the palladium-catalyzed coupling reaction of vinyl halides with Grignard reagents,[13,14] alkyl lithium,[15,16] organozinc,[17] organoaluminum[18] and organozirconium[19,20] reagents, the olefin retains its geometrical integrity, presumedly as a result of retention both in the oxidative addition and reductive elimination steps.



We have shown by nmr that the oxidative addition of both cis- and trans-β-bromostyrene to tetrakis(phosphine)palladium(0) complexes takes place with retention of geometry. The reaction of these palladium(II) complexes with methyl lithium gives cis- and trans-propenylbenzene respectively, in high yields in 100% isomeric purity. Free phosphine must be present for the coupling reaction to take place in high yields.



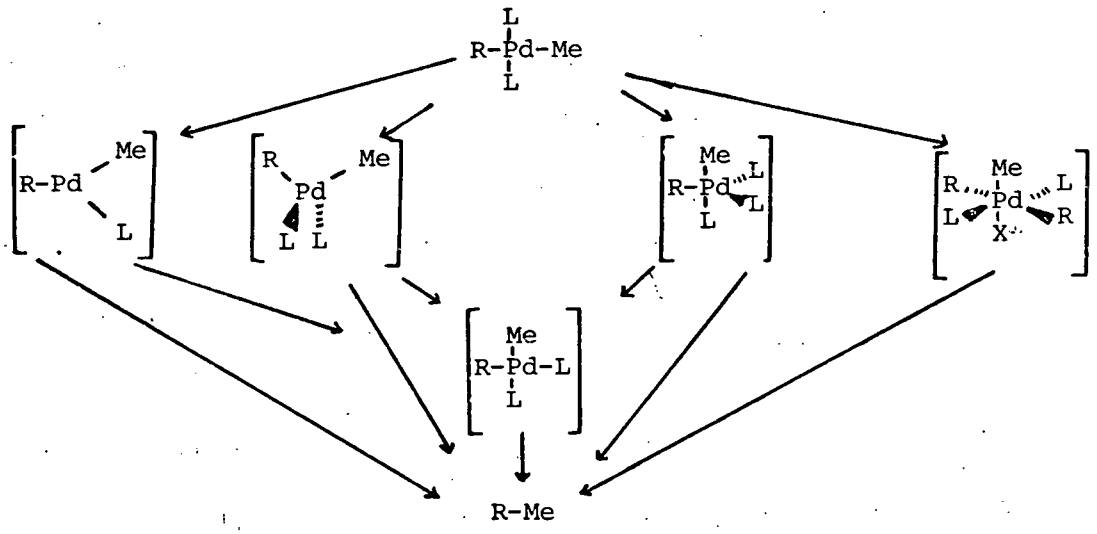
We have succeeded in the isolation of the intermediate styryl methyl palladium complex, by the low temperature reaction of bromo-trans-styrylbis-(diphenylmethylphosphine)palladium(II) with methyl lithium. A mixture of the cis- and trans-complex is obtained. When this mixture is allowed to warm up in $CDCl_3$, the decomposition can be followed by nmr (^1H, ^{13}C, and ^{31}P), showing the generation of propenyl benzene.



Reductive Elimination of Ethane from Dimethyl Palladium Complexes. The results with the reductive elimination reactions of styrylmethylpalladium(II) and benzylmethylpalladium(II) complexes raises some important questions. The reductive elimination reactions of the various diorganopalladium complexes has been assumed to require a cis-geometry of the coupling groups. If the reductive elimination reaction does indeed require a cis-arrangement of the departing fragments, then the arrangement of the leaving group is important. This can occur by several processes: 1) Oxidative addition to the palladium(II) complex to form a palladium(IV) complex in which the

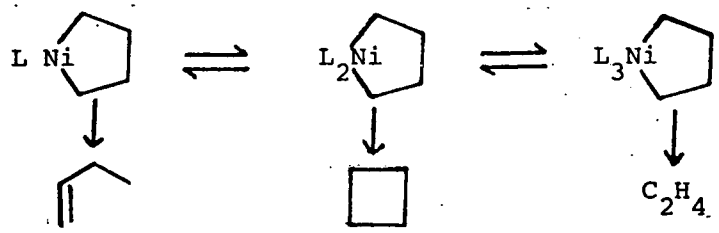
two leaving groups can achieve adjacent positions, 2) Prior dissociation of a phosphine to give a three-coordinate intermediate (dissociative mechanism) 3) Prior association of a phosphine to give a trigonal bipyramid (fluxional) in which the departing partners can be adjacent (associative mechanism) 4) Conversion of the complexes in 2 or 3 to the cis-complex by the recoordination or dissociation, respectively, of a phosphine and 5) Distortion of the trans complex into a transient tetrahedral geometry (Scheme II).

Scheme II



Nickel catalyzed the coupling of Grignard reagents with organic halides,[21] and the oxidative addition-metathesis-reductive elimination steps have been documented separately.[22,23] Because 1, the catalytic reaction takes place more rapidly than the isolated reductive elimination step, 2, the reductive elimination is intramolecular, 3, the trans complex is the only one observed, and 4, added phosphine retards the reactions, a dissociative mechanism appears to be the most viable, at least in the isolated step. However, the elimination has been reported to be facilitated by olefins[24]--especially those bearing electronegative substituents--and other electron acceptors.[25] Consequently,

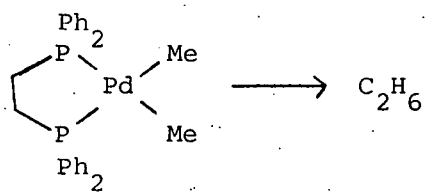
a radical cation mechanism has been suggested.[26] The mode of elimination from nickelacyclopentanes (β-H, 1,1- or β-C, see below) depends on the number of coordinated phosphines.[27] In this case, cis geometry is imposed and β-H elimination is surpressed by the unfavorable conformation.



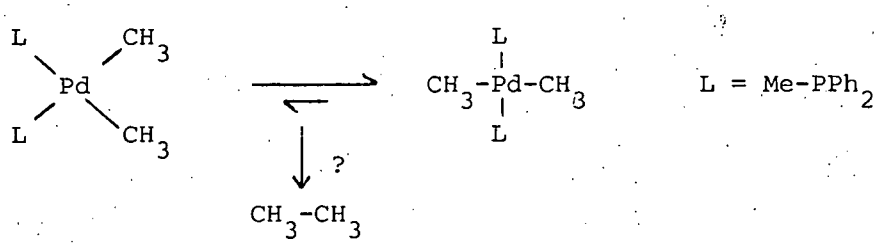
Diorganoplatinum(II) compounds that do not contain β-hydrogens are relatively stable,[31] even above room temperature.[32] The reductive elimination proceeds by a concerted, intramolecular reaction of cis-groups.[33] Since phosphine enhances the rate of elimination, this can be interpreted as an associative mechanism. The rate of reductive elimination of methane from hydridomethylplatinum(II) complexes, however, is unaffected by added phosphine.[34] Platinacyclobutanes and dineopentyl platinum complexes that do not undergo β-elimination reactions readily, give a variety of intramolecular decomposition products.[35-37] In inert solvents, the rate of elimination is enhanced by added phosphine. In methylene chloride, oxidative addition of the solvent takes place, and reductive elimination occurs from a platinum(IV) complex to give predominately cyclobutane. This 1,1-elimination pathway from platinum(IV) complexes is well documented.[31,38,39] Palladacyclopentane complexes also have been shown to possess enhanced stability toward any elimination mode.[40]

We have synthesized a number of cis- and trans- dimethylbis(phosphine)-palladium(II) complexes and followed their isomerization and decomposition in solution by nmr. The product of decomposition in all cases is ethane.

When the phosphine is a chelating phosphine such as diphos, and no isomerization to the trans complex can take place, ethane is readily produced and no methane could be detected.

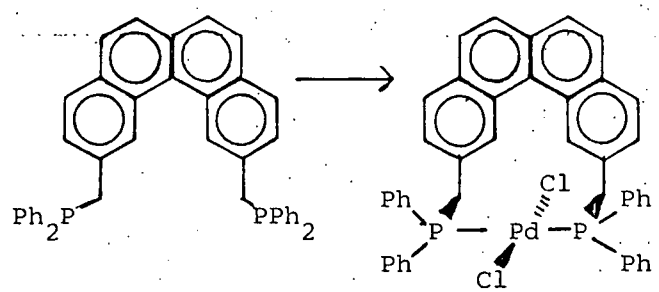


In an inert solvent such as benzene, no cis-trans-isomerization of dimethylbis(diphenylmethylphosphine)palladium(II) takes place and no reductive elimination occurs, even at temperatures up to 50°C. The addition of phosphine causes rapid isomerziation of the cis-isomer to the more stable trans-isomer, even at 25°. Reductive elimination takes place in this case,



at 25° but more rapidly at 50°C. Coordinating solvents such as tetrahydrofuran or chloroform also allow isomerization (25°) and reductive elimination (50°) to take place. This suggest that an associative mechanism is operative, although it is not clear whether reductive elimination could take place from the cis complex in the absence of phosphine (as apparently does happen when diphos is the ligand). Also, it is not clear whether coordination from solvent or phosphine to either isomer or only one of the isomers is occurring as a necessary pathway to reductive elimination.

To answer this question, we will study the elimination reactions from complexes that must retain one isomeric structure. Diphos provides this for the cis case. We have synthesized, therefore, a trans-bridging phosphine[41] for comparison. A complex of this phosphine with palladium chloride has been prepared in order to convert it to the dimethylpalladium species.



Effort of Principal Investigator

Approximately 15% of the time of the principal investigator was devoted to the project. The same percentage of effort is expected to be expended during the remainder of the current term.

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* References 10 and 11 report work supported by this grant.