

Triarylphosphine-Palladium Complexes

CATALYSTS FOR THE FORMATION OF CARBON-CARBON BONDS

By Richard F. Heck

Department of Chemistry, University of Delaware, Newark, Delaware, U.S.A.

Aryl, heterocyclic, benzyl, and vinylic halides undergo facile reactions with carbon monoxide or olefins forming new carbon-carbon bonds under the influence of triarylphosphine-palladium catalysts. The carbon monoxide reactions produce esters in the presence of alcohols, amides in the presence of amines, and aldehydes in the presence of hydrogen. Reactions with olefins produce new olefins in which a vinylic hydrogen is replaced by the organic group from the halide. Some olefins and vinylic halides require the presence of secondary amines to react, in which instance tertiary allylic amines are formed catalytically. Conjugated dienes may be used in place of simple olefins to form products with additional unsaturation. Numerous applications for these reactions in organic synthesis appear likely.

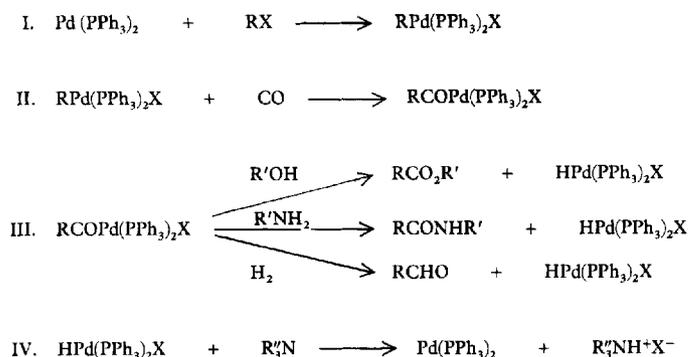
The formation of carbon-carbon bonds is the most important reaction in organic chemistry. While a very large number of methods have been developed to accomplish this reaction, it has been relatively recently that methods involving transition metals as catalysts have been discovered. Even in this relatively small area of chemistry, numerous promising reactions have been found. Of the few of these that are broadly useful, perhaps palladium catalysed reactions will eventually prove to be the most important. The chemical step which makes palladium so useful is the facile addition of various organopalladium complexes to carbon monoxide and to carbon-carbon double bonds to form new carbon-carbon bonds. To be useful in catalytic reactions this step must be coupled with an initial step forming the organopalladium complex and a final step in which the palladium is lost from the adduct in a reusable form. Palladium readily brings about these reactions homogeneously when various organic halides are reacted with triarylphosphine-palladium catalysts in the presence

of tertiary, or in some instances secondary, amines and an additional reagent in the case of the carbon monoxide reactions. We have generally employed one mole per cent of the palladium catalyst based upon the organic halide used, but smaller amounts probably would be sufficient in most reactions.

Carbonylation of Organic Halides

Organic halides may be converted into esters (1), amides (2) or aldehydes (3) with one additional carbon atom by means of triarylphosphine-palladium catalysts. Generally, triphenylphosphine has been used as the stable dichloro- or dibromobis(triphenylphosphine)palladium(II) complex. These complexes are readily reduced under the reaction conditions, about 100°C, to the active catalyst which is probably bis(triphenylphosphine)palladium(0). The last complex then reacts with the organic halide to form organobis(triphenylphosphine)halopalladium(II) derivatives. It is these species that form the new carbon-carbon bond by adding to carbon monoxide thus creating an

acyl-palladium complex. This complex then is reacted with either an alcohol to form an ester, an amine to form an amide, or hydrogen to produce an aldehyde. In all three reactions the palladium is converted into a hydridobistriphenylphosphinehalopalladium(II) complex. Fortunately, these hydrides readily dissociate into hydrogen halide and the active catalyst, bistrisphenylphosphinepalladium(0). The catalyst is totally recycled if a basic tertiary amine, or in the case of the amide reaction the primary or secondary amine being used in the reaction, is present to neutralise the hydrogen halide formed. The formulation of the proposed reactions is as follows:



Two important limitations of the reactions are that organic iodides and bromides generally react better than chlorides and the organic group must be an aryl, heterocyclic, benzylic or vinylic group. Alkyl halides with beta hydrogens produce only olefins under the reaction conditions which are 60 to 130°C with one atmosphere of carbon monoxide. Higher pressures of hydrogen are necessary in the aldehyde synthesis. Advantages of the reactions include good to excellent yields of products, retention of stereochemistry in vinylic halide reactions, and tolerance of the reaction to a wide variety of functional groups.

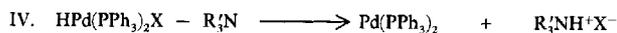
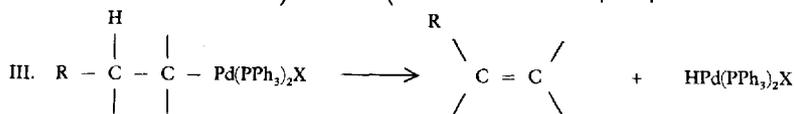
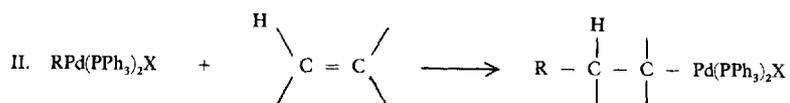
Formation of Carbon Bonds to Vinylic Carbons

The same organopalladium complexes which add to carbon monoxide also add to carbon-carbon double bonds. If at least one vinylic or allylic hydrogen is present in the unsaturated

compound, the adduct may have the hydrogen on a saturated carbon, beta to the palladium group. In this circumstance, rapid elimination of a hydridopalladium group occurs resulting in the formation of a new carbon-carbon bond between the organic group initially on the palladium and one of the original double bond carbons. This reaction is easily made catalytic in palladium by forming the organopalladium complex from an organic halide and the presumed palladium(0)-triarylphosphine complex formed by in situ reduction of a palladium(II)-triarylphosphine complex. The catalytic cycle is completed as in the carbonylation reactions, by inclusion of a basic tertiary amine

in the reaction mixture to convert the hydrido-palladium product back to the palladium(0)-triarylphosphine catalyst. In this reaction we prefer to add the catalyst in the form of diacetatobistriphenylphosphinepalladium(II) rather than as the halide because of its higher solubility in the reaction mixtures (4). When the less soluble halide catalyst is used, careful initial warming and stirring is necessary to convert it into the active homogeneous form without partial loss because of the formation of palladium metal; the relevant reactions being given at the top of the next page.

The same limitations on the organic halide and the same advantages as observed in the carbonylation are found here also; similar reaction conditions also are employed. Additions to unsymmetrical olefins generally result in the organic group adding to the least substituted vinylic carbon and/or beta to strongly electron-withdrawing substituents, the addition being

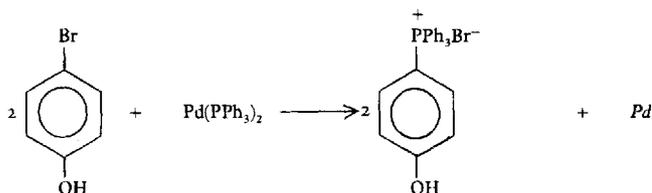


stereospecific. The major stereoisomer arises from a *syn* addition of the organopalladium group followed by a *syn* elimination of the palladium hydride (4).

The triarylphosphine employed in the catalyst is generally not critical except in the reactions of aryl bromides possessing strongly electron donating substituents such as hydroxyl or amino groups. In these reactions with triphenylphosphine in the catalyst, tetraarylphosphonium bromides are rapidly formed in a side reaction causing decomposition of the catalyst to inactive palladium metal.

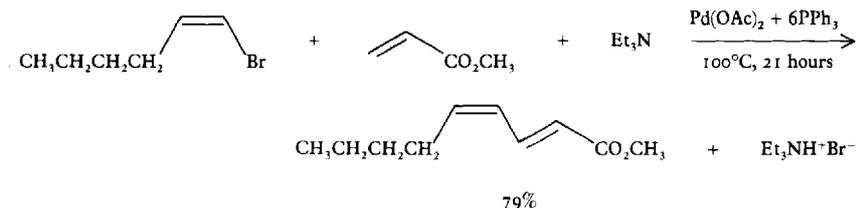
Secondary amines such as piperidine often may be used in place of the triarylphosphine and also as the basic reagent to react with the hydrogen halide. The phosphine or secondary amine are necessary to cause organic bromides to react but most iodides will react without these ligands being present. This allows the selective reaction of iodo substituents in the presence of bromide groups.

Most aryl (6) and heterocyclic (7) bromides and iodides react normally according to the above scheme. However, some vinylic halides require special conditions to react catalytically



The side reaction can be eliminated by using the hindered tri-*o*-tolylphosphine instead of the phenyl compound (5). An excess of the phosphine over the two equivalents per

under which different products are formed. Acrylonitrile, acrylic acid and its esters react normally with vinylic halides forming conjugated dienes (8). For example:

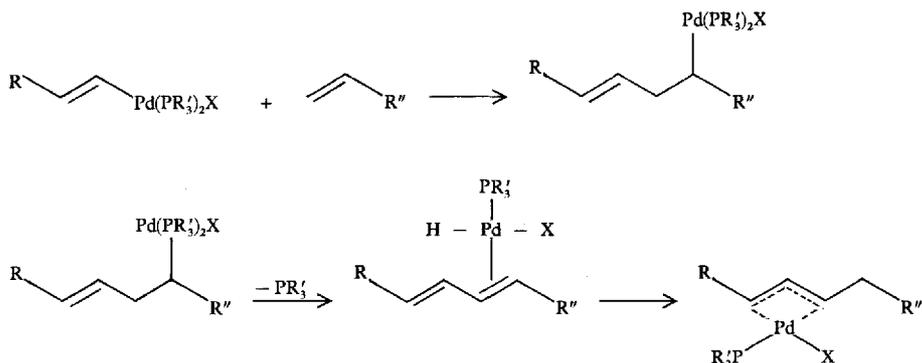


palladium normally used sometimes improves yields also in reactions when catalyst decomposition to palladium metal occurs. Trialkylphosphines or triorgano phosphite esters are not generally useful in this reaction.

Olefins without the activating nitrile or carboxyl function, however, react very slowly or not at all under these conditions. The problem is that relatively stable π -allylic palladium halide complexes are formed. The initial adduct

of the vinylic palladium halide with the olefin apparently undergoes beta hydride elimination but instead of dissociating, the hydride adds back to the newly formed double bond in the reverse direction giving the allylpalladium derivative.

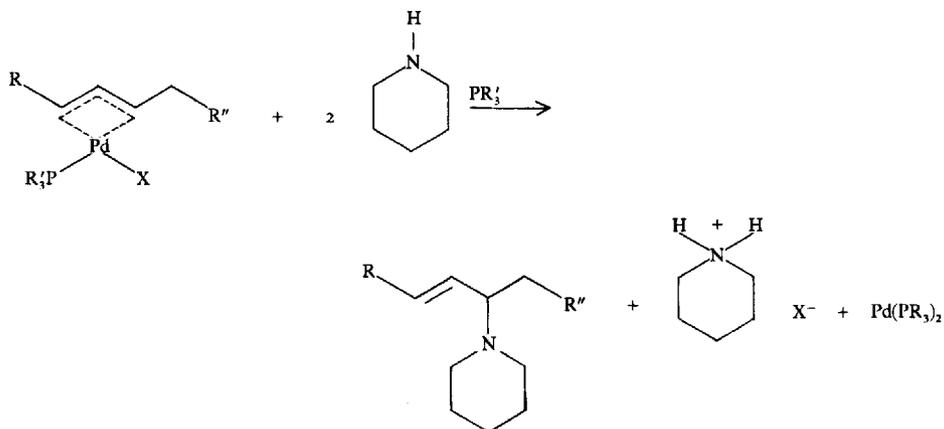
Either or both of two isomeric allylic amines may be formed by displacement at either end of the allylic group but often the reaction is quite selective towards a single isomer depending upon the substituents present. This is a remarkable reaction producing relatively complex

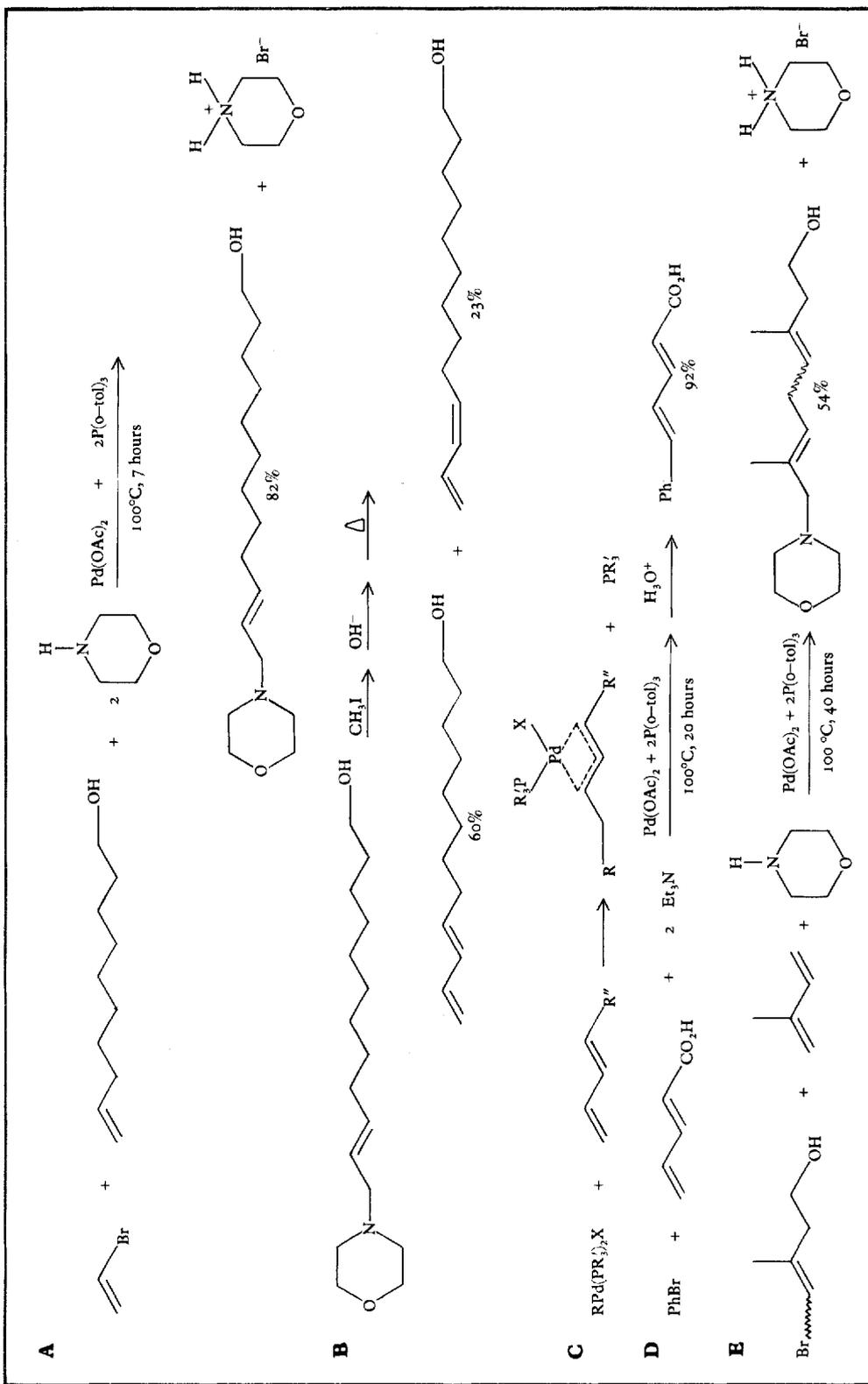


If the R'' group in the above equations is a nitrile or carboxyl group, the alpha hydrogens are acidic enough to be removed by the tertiary amine present and cause elimination of the palladium and produce a catalytic cycle. However, in the absence of the acidifying group the complexes are quite stable to the tertiary amine. It has been found that these complexes can be caused to lose the palladium if a nucleophilic secondary amine is used in place of the tertiary amine. The palladium is now displaced and a tertiary allylic amine is formed. The reaction is catalytic because the displacement reforms the palladium(o)triarylphosphine catalyst or in the absence of a phosphine, a secondary amine palladium(o) complex (9).

molecules from simple components under convenient, mild conditions in moderate to high yields. Its broad synthetic utility is obvious since the amine function may easily be removed or replaced by well-known reactions such as the Hofmann elimination, hydrogenolysis or von Braun type reactions. For example, 9,11-dodecadienol, the pheromone of the Red Bollworm Moth, was prepared in good yield from vinyl bromide and 9-decenol, the reactions being given as **A** and **B** on page 62.

A variation of the reaction occurs when conjugated dienes are used in place of simple olefins. π -Allylic palladium halide intermediates are believed to be formed directly in these reactions, see **C**.





As expected from the above results if R" is a carboxyl group, basic tertiary amines bring about a catalytic reaction (10). For example, 5-phenyl-2,4-pentadienoic acid is obtained in over 90 per cent yield from bromobenzene and 2,4-pentadienoic acid as given in D, page 62.

Vinyllic halides also react with dienes but in the absence of nitrile or carboxyl substituents, secondary amines are required which produce tertiary allylic amines and cause catalytic reac-

tions. Terpene derivatives have been produced by this reaction (11). An example is given in E on the previous page.

These few examples illustrate the extraordinary ability of palladium to produce carbon-carbon bonds selectively. Since these reactions often cannot be achieved as easily in other ways, palladium catalysis should become a useful addition to the synthetic methods available to the organic chemist.

References

- 1 A. Schoenberg, I. Bartoletti and R. F. Heck, *J. Org. Chem.*, 1974, **39**, (23), 3318
- 2 A. Schoenberg and R. F. Heck, *J. Org. Chem.*, 1974, **39**, (23), 3327
- 3 A. Schoenberg and R. F. Heck, *J. Am. Chem. Soc.*, 1974, **96**, (25), 7761
- 4 H. A. Dieck and R. F. Heck, *J. Am. Chem. Soc.*, 1974, **96**, (4), 1133
- 5 C. B. Ziegler, Jr. and R. F. Heck, *J. Org. Chem.*, 1978, **43**, (15), 2941
- 6 B. A. Patel, C. B. Ziegler, Jr., N. A. Cortese, J. E. Plevyak, T. C. Zebovitz, M. Terpko and R. F. Heck, *J. Org. Chem.*, 1977, **42**, (24), 3903
- 7 W. C. Frank, Y. C. Kim and R. F. Heck, *J. Org. Chem.*, 1978, **43**, (15), 2947
- 8 H. A. Dieck and R. F. Heck, *J. Org. Chem.*, 1975, **40**, (8), 1083
- 9 B. A. Patel and R. F. Heck, *J. Org. Chem.*, 1978, **43**, (20), 3898
- 10 B. A. Patel, J. E. Dickerson and R. F. Heck, *J. Org. Chem.*, 1978, **43**, (26), 5018
- 11 B. A. Patel, L.-C. Kao, N. A. Cortese, J. V. Minkiewicz and R. F. Heck, *J. Org. Chem.*, 1979, **44**, (6), 918

Catalyst Availability

The following five U.S. Patents have been granted on various aspects of the technology outlined in this article by Professor Richard F. Heck: 3,922,299; 1975, 3,960,932; 1976, 3,988,358; 1976, 4,128,554; 1978 and 4,175,187; 1979

Licensing is available through Johnson Matthey Inc. For further information and experimental samples of catalysts contact Dr. Ernest Gore, Johnson Matthey Incorporated, 1401 King Road,

West Chester, PA 19380, U.S.A. (Telephone 215/648-8000). Quotations for commercial size quantities are available.

In addition to the reactions described above, compounds of the type Pd(PR₃)₂Cl₂ have many other catalytic uses, for example, hydrosilylation, synthesis of long chain carboxylic acids and esters, and the addition of alkyl and aryl halides to alkynes. Further information is available on request.

A Possible New Mining Area for Rustenburg

The major commercial platinum metals deposits in South Africa occur in the enormous geological formation known as the Bushveld Igneous Complex. Since their discovery in the 1920's these deposits have become increasingly important and they now form the principal source of platinum metals for the Western World. In addition these are the only deposits primarily worked for platinum, thus the mines located on them are able to respond most rapidly to an increase in demand for the metal.

Continuing its exploration of the Bushveld Igneous Complex as part of its evaluation of possible future mining areas, Rustenburg

Platinum Mines reports that particular emphasis is being placed on the so-called Merensky Platereef of the Potgietersrust district that was originally mined in the 1920's. Prospecting results to date indicate that this area has the potential for supporting a major new platinum, nickel and copper mine.

Indications are that this wide ore-body might be exploitable by open-cast methods at working costs below those of conventional underground mining, but much work remains to be done in evaluating this deposit, particularly as its metallurgical characteristics differ from those of the deposits mined in current operations.