Tetrahedron Vol. 40, No. 13, pp. 2415 to 2434, 1984
Printed in Great Britain.

0040-4020/84 $5.00 + .00
Pergamon Press Ltd.

TETRAHEDRON REPORT NUMBER 166

PALLADIUM(II)-ASSISTED REACTIONS OF MONOOLEFINS

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(*Received in the USA* 6 *June* 1983)

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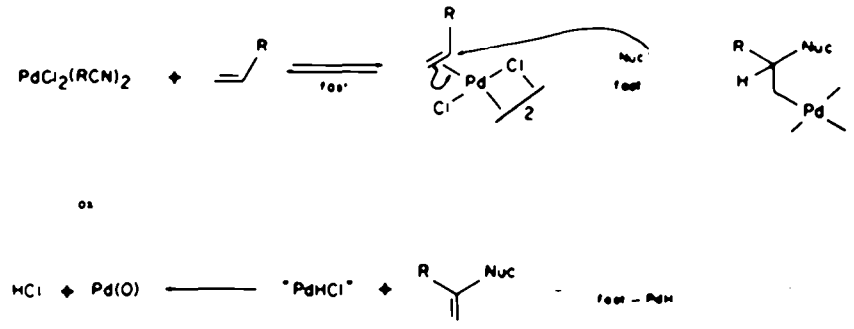
Among the transition metals, palladium is one of the most extensively used for the synthesis of both industrial and fine chemicals. The reasons are partly historical (the Wacker process for the palladium-catalyzed oxidation of ethylene to acetaldehyde was developed twenty five years ago) and partly due to the versatility, availibility, and utility of organopalladium complex chemistry. Particularly useful are the reactions of olefins catalyzed by palladium(II) complexes. These comprise two major reaction types, nucleophilic attack on palladium(II) complexed olefins, and insertions of olefins into σ-alkylpalladium(II) species. Both processes will be discussed in this review.

Nucleophilic attack on mono-olefinpalladium(II) complexes

The most common commercially available palladium(II) salt is palladium chloride which, unfortunately, is virtually insoluble in most organic solvents. However, palladium chloride is readily converted to a number of soluble palladium(II) species including Na_2PdCl_4,[1] $PdCl_2(PhCN)_2$,[2] and $PdCl_2(MeCN)_2$.[3] These, along with palladium acetate, which is soluble in benzene and alcohols, are the most commonly used palladium(II) salts for the chemistry discussed below.

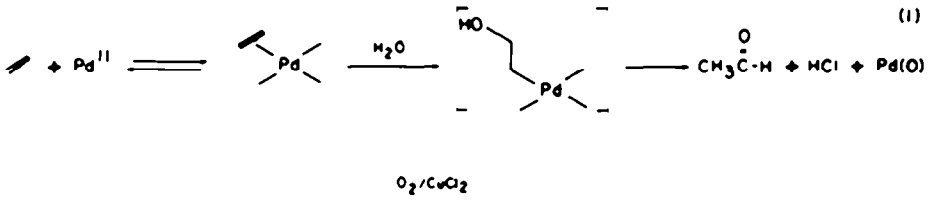
In organic solvents, palladium(II) salts *rapidly* coordinate mono-olefins to form π-olefinpalladium(II) halide dimers. Ethylene and terminal mono-olefins coordinate most effectively, followed by *cis* and *trans*-disubstituted olefins. Under normal circumstances geminally disubstituted, trisubstituted, and tetrasubstituted olefins do not coordinate sufficiently well to permit further chemistry, nor do electrophilic olefins. Once coordinated to palladium, the olefin is generally subject to nucleophilic attack, which occurs rapidly, and predominantly at the more substituted position of the olefin, forming a carbon-nucleophile bond and a carbon–palladium bond. In most instances this attack occurs from the face opposite the metal, and without prior coordination of the nucleophile, although this is dependent on the nature of the nucleophile. The thus-formed σ-alkylpalladium species is quite unstable and undergoes a rapid, spontaneous β-hydride elimination to form the substitution product and "PdHCl", which decomposes to palladium(O) and HCl. In the presence of suitable reoxidants ($CuCl_2$, benzoquinone, $K_2S_2O_8$, $FeCl_3$) the palladium(O) is reoxidized to palladium(II), and can reenter the catalytic cyclic (Scheme 1). Since olefin complexation, nucleophilic attack, β-elimination, and reoxidation all occur rapidly, palladium(II) salts are effective catalysts for a number of important nucleophilic substitution processes with olefins.



Scheme 1.

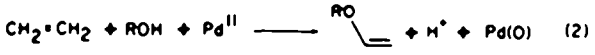
Reaction of oxygen nucleophiles with π-olefinpalladium(II) complexes

Among the earliest-developed palladium(II) catalyzed reactions of olefins was the Wacker process for the "oxidation" of ethylene to acetaldehyde (eqn 1). Although after twenty five years



(1)

the mechanism of this process is still controversial,[4] it is clear that the key step involves nucleophilic attack of water on the palladium-bond olefin. Alcohols[4,5] and acetate[4,5] react similarly to produce enol ethers and vinyl acetate respectively (eqns 2 and 3). In virtually all cases air and copper(II)



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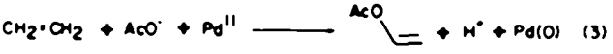
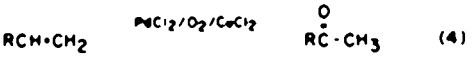


(3)

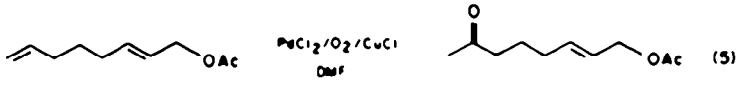
salts are used to carry the palladium redox chemistry, and many of these processes have been commercialized.

With longer chain mono-olefins, attack occurs exclusively at the more substituted position, producing ketones when water is the nucleophile (eqn 4). The reaction is quite specific and readily



(4)

distinguishes between terminal and internal olefins, and, in addition, tolerates a variety of remote functional groups. This reaction is particularly useful for the further functionalization of butadiene telomers (eqns 5 and 6),[6,7] and has been used in the synthesis of polycyclic materials (eqn 7).[8] Allyl ethers undergo a similar reaction (eqn 8).[9]



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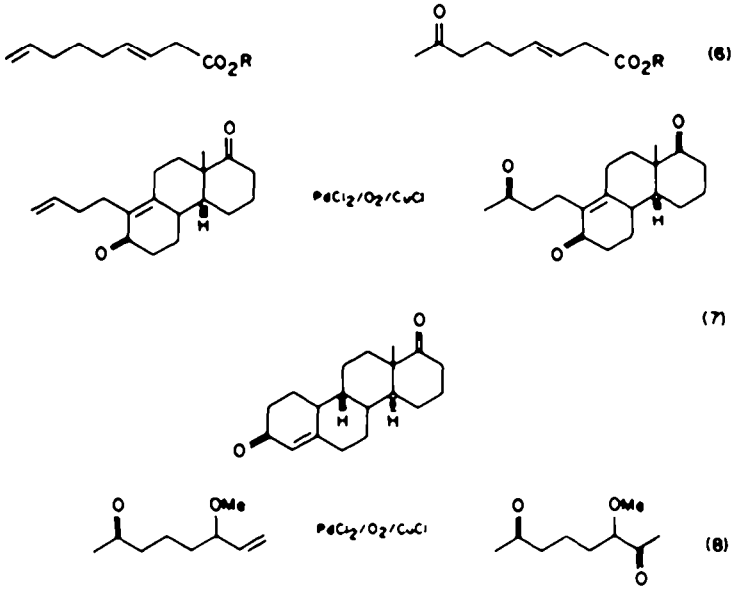
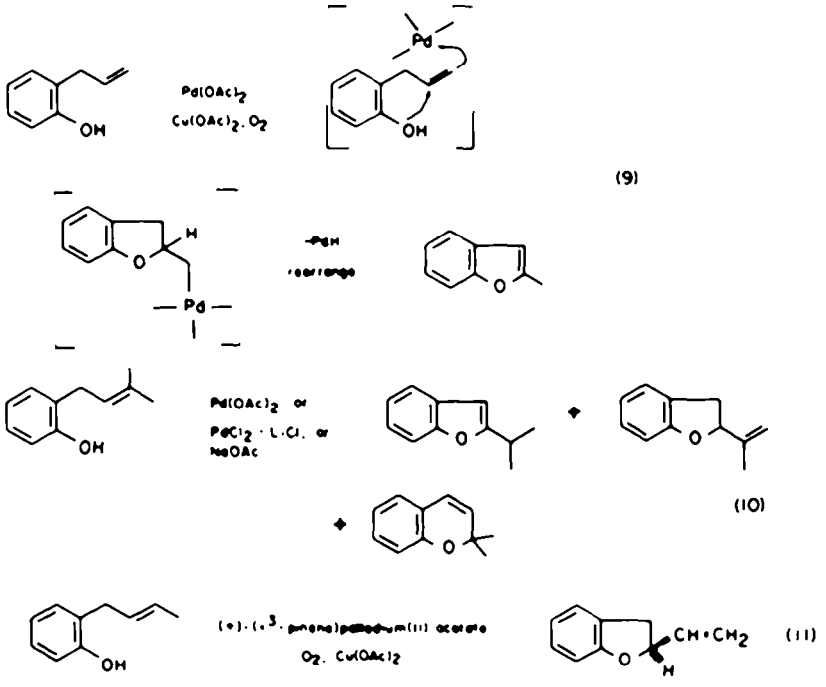
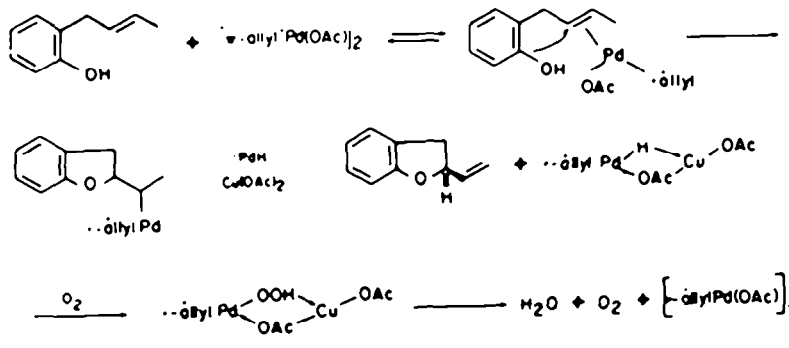


Intramolecular versions of these processes have proven particularly useful for the synthesis of oxygen heterocycles. 2-Allylphenol itself cyclizes to 2-methylbenzofuran in fair yield, and is likely to proceed as shown in eqn (9).[10] In contrast phenols with methyl-substituted allyl groups cyclized to a variety of five and six membered ring products, the composition of which depends on the palladium(II) salt ($PdCl_2$ or $Pd(OAc)_2$) and the amount of added chloride or acetate (eqn 10).[11,12]

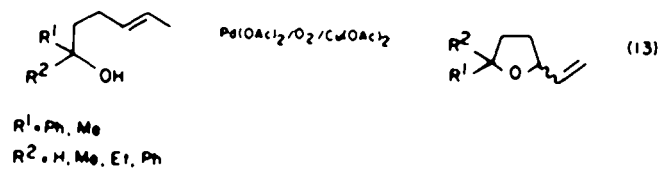


Most remarkably, use of a chiral π-allylpalladium complex as a catalyst for this reaction with *trans*-2-(2-butenyl)phenol as substrate produces 1,3-dihydro-2-vinylbenzofuran in up to 18% optical purity (eqn 11).[13] This requires that the palladium remain coordinated to the π-allyl group *throughout the catalytic cycle*, and thus the expected β-hydride elimination, and loss of HCl to form palladium(0) must not occur in this case. Instead, a mechanism involving *direct* oxidation of a bimetallic palladium(II) hydride-copper(II) species by oxygen is proposed (eqn 12), a fundamentally new oxidative process for palladium(II)-catalyzed reactions.

(12)



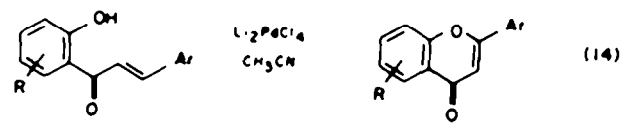
A variety of other olefinic alcohols cyclize in the presence of palladium(II) catalysts to form interesting oxygen heterocycles (eqns 13–15). Particularly interesting is the elegant synthesis of brevicomin by this method (eqn 15; which may, however, involve oxidation of the olefin to a ketone followed by ketal formation rather than direct hydroxylation of the olefin)



(13)

R^1 = Ph, Me

R^2 = H, Me, Et, Ph



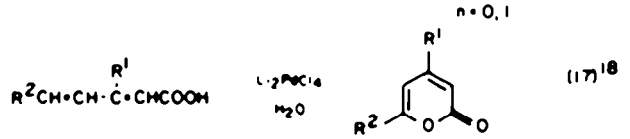
(14)

(15)[16]

Intramolecular reactions in which the nucleophile is a carboxylate ion are also quite efficient, and produce unsaturated lactones (eqns 16–18). Although most of these particular reactions were carried out using stoichiometric amounts of palladium, a few have been carried out catalytically, and catalytic processes should be feasible for all of them.

(16)[17]

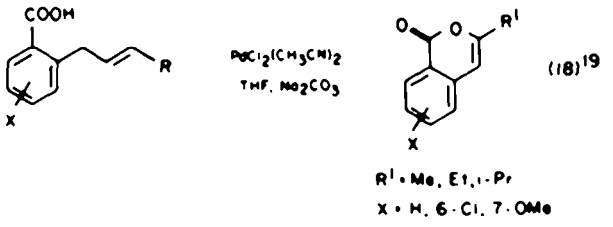
n = 0, 1



(17)[18]

R^1 = H, Me, Ph

R^2 = H, Me, Ph

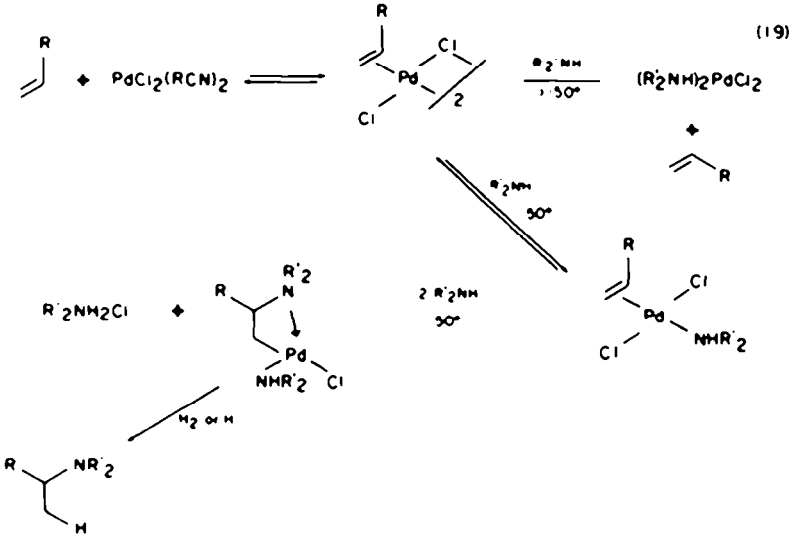


(18)[19]

Reactions of nitrogen nucleophiles with π-olefinpalladium(II) complexes

The overwhelming success of the Wacker and related processes involving oxygen nucleophiles led to the mistaken belief that most classes of nucleophiles would react effectively with palladium(II)-bound olefins. However, only very recently have nitrogen and carbon nucleophiles been successfully used to aminate and alkylate palladium(II) olefin complexes. Oxygen nucleophiles are somewhat unusual in that they coordinate only weakly to palladium(II) compounds, and, in general, do not compete with olefins for a coordination site on the metal. In contrast, amines and most other nitrogen nucleophiles are excellent ligands for palladium(II) and readily displace (rather than attack) olefins from the metal. Thus the intermolecular amination of olefins was difficult to achieve, and, because both starting amine and product enamine are potent ligands for palladium, the intermolecular amination of olefins has not yet been achieved catalytically.

The stoichiometric amination of olefins (eqn 19) has several interesting features.[20] The reaction

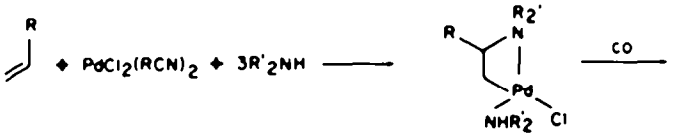


(19)

must be carried out at low temperatures ($\sim -50°$) with slow addition of amine to the preformed olefinpalladium(II) complex, to prevent displacement from the metal of olefin by amine. Three equivalents of amine are required to achieve reasonable yields of amination. No carbon–nitrogen bond formation is observed after the addition of one equivalent of amine, and less than 30% amination is observed after addition of two equivalents of amine. Addition of the third equivalent of amine results in amination in greater than 90% yield. This suggests that nucleophilic attack is occurring on a palladium–olefin–amine complex rather than on the olefin-palladium dimer itself, although the exact nature of this intermediate has not yet been determined. After addition of the third equivalent of amine, the relatively unstable β-aminoalkylpalladium complex (isolated and characterized by NMR)[21] is the sole organopalladium species present, reduction of which by hydrogen or hydride produces amine in excellent yield.

This amination reaction proceeds best with nonhindered secondary amines and terminal olefins. Primary amines and internal olefins react somewhat less efficiently ($\sim 50\%$ yield), while trisubstituted olefins react in very low yield, as does ammonia. The stereochemistry of amination is cleanly *trans* with attack occurring from the face opposite the olefin, without prior coordination to the metal.[22] Regioselective attack at the most substituted position of the olefin, also consistent with external nucleophilic attack, is also observed.

In principle, the above chemistry offers an efficient route for the direct amination of unactivated olefins, a transformation not accessible to conventional organic chemistry. However, because it requires stoichiometric amounts of palladium, its practical utility is limited to the synthesis of compounds simply not available by other routes. More useful, perhaps, are further transformations of the unstable β-aminoalkylpalladium(II) intermediate from the amination reaction. In common with most σ-alkylpalladium(II) complexes, the β-aminoalkylpalladium intermediate undergoes a



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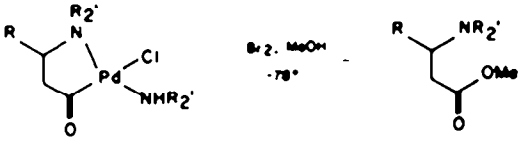
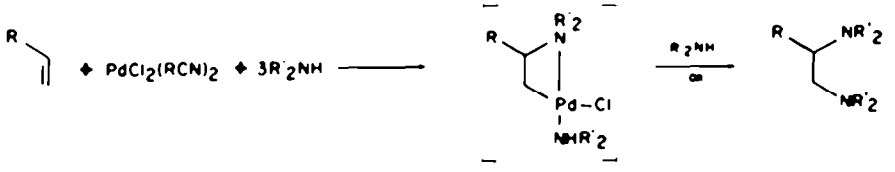


variety of useful insertion and oxidative cleavage reactions. Exposure of this complex (formed *in situ* and not isolated) to an atmosphere of carbon monoxide produces a very stable five-membered chelate β-aminoacyl palladium complex[23] which undergoes oxidative cleavage to produce β-aminoacid derivatives in good yield (eqn 20).[24] Oxidation of the β-aminoalkyl complex in the presence of other nucleophiles results in the overall diamination or oxamination of the original olefin (eqn 21).[25] The process is stereospecific, proceeding with overall *cis* stereochemistry resulting from a *trans*-amination of the olefin followed by nucleophilic displacement of the (oxidized) palladium with inversion. Bromine, lead tetraacetate, and N-bromosuccinimide are all efficient oxidants for this process. Aryl ethers oxaminate under these conditions to give fair yields of highly functionalized products (eqn 22).[26] By using a chiral tertiary amine as a ligand, and a chiral secondary amine as the nucleophile olefins are oxaminated in modest yield in up to 60% ee (eqn 23).[27] If an achiral secondary amine is used as the nucleophile, only 3–11% ee is observed. Applying this process to aryl allyl ethers leads to modest optical induction (11% ee) (eqn 24).[28] Use of a primary amine as nucleophile, followed by an intramolecular oxidative cleavage, produces azirdines in modest yield (eqn 25).[29]



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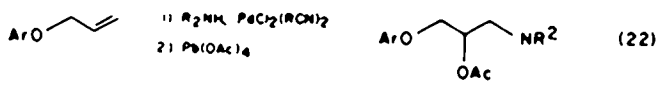

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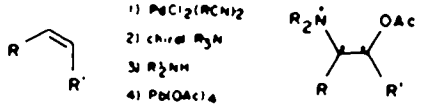

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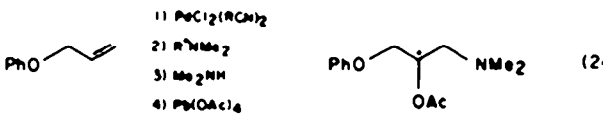

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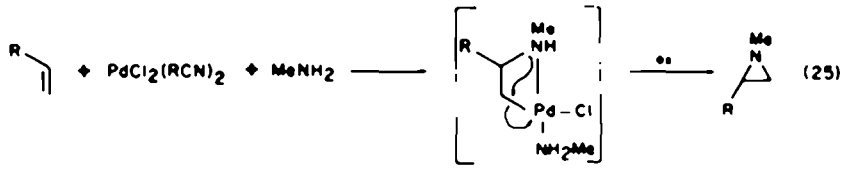

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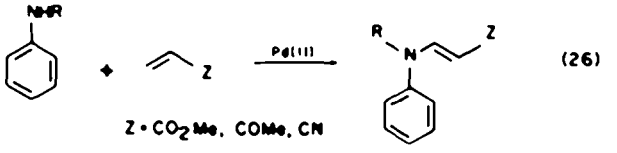

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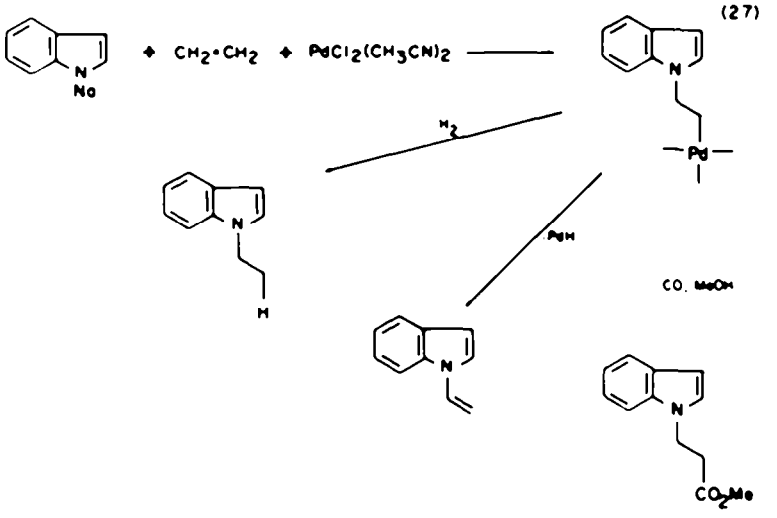
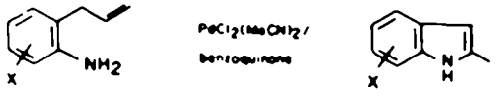


Other, miscellaneous, palladium-assisted aminations of olefins are shown in eqn (26),[30] and (27).[31]

In contrast to the difficulties encountered with intermolecular amination of olefins, *intramolecular* processes are considerably more facile and a number of useful catalytic nitrogen heterocyclization reactions have been developed. Indoles form readily from 2-allylaniline using a palladium(II) catalyst and benzoquinone as the reoxidant for palladium (eqn 28).[32] (Since both anilines and indoles are relatively easily oxidized, the usual copper(II) oxidizing systems resulted in destruction of the product.) With alkylated side chains, amination occurs at the most substituted terminus (eqn 29). These reactions also proceed through an unstable σ-alkyl palladium complex, which readily inserts carbon monoxide to give the corresponding ester. Conjugated enones also insert (eqn 30).[33] When a conjugated enone is built in to the allyl aniline system, tricyclic material



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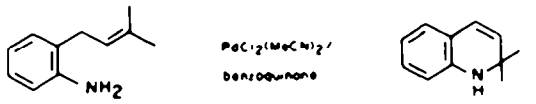

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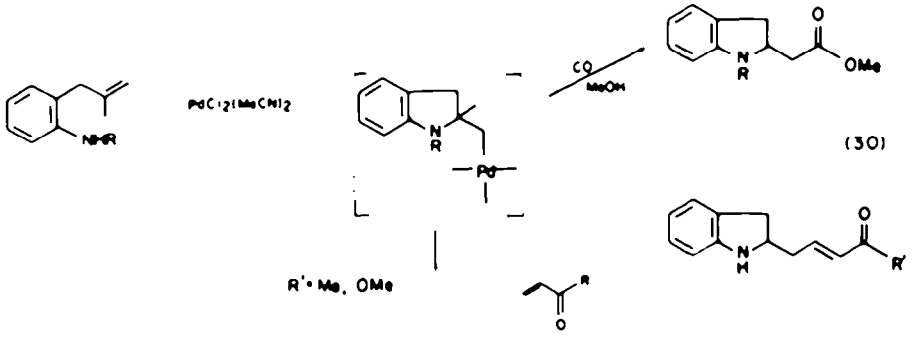
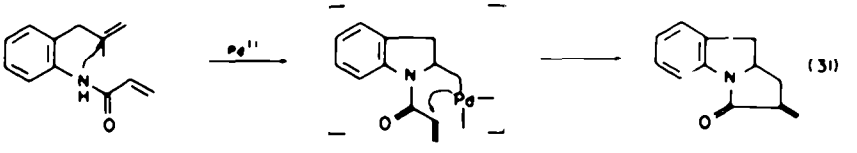


(30)

results in excellent yield (eqn 31). The change in regiochemistry of the insertion step (α-alkylation rather than the normal β-alkylation) is likely due to steric constraints as a consequence of the intramolecular nature of the reaction.

Extension of this heterocyclization reaction to aliphatic amino-olefins proved to be rather difficult. Aliphatic amines are $\approx 10^6$ more basic than aromatic amines, and they coordinate more strongly to palladium(II) complexes than do their aromatic counterparts. Thus treatment of the amino-olefin in eqn (32) with palladium(II) salts results in the formation of stable olefin-amine-palladium(II) complexes. Since the amine nitrogen is strongly coordinated to the metal, it cannot attack the coordinated olefin. This problem can be overcome by conversion of the free amine to its tosamide. These crystalline substrates readily cyclize in the presence of catalytic amounts of palladium(II), and with benzoquinone as the reoxidant, to form unusual cyclic tosylated enamines (eqns 33–35).[34] Reduction followed by photolytic detosylation gives the free cyclic amine in good yield.



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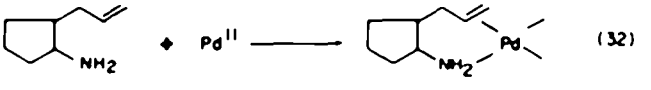

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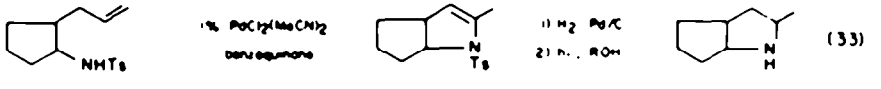

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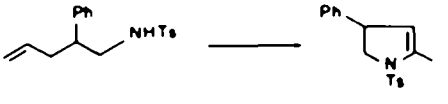
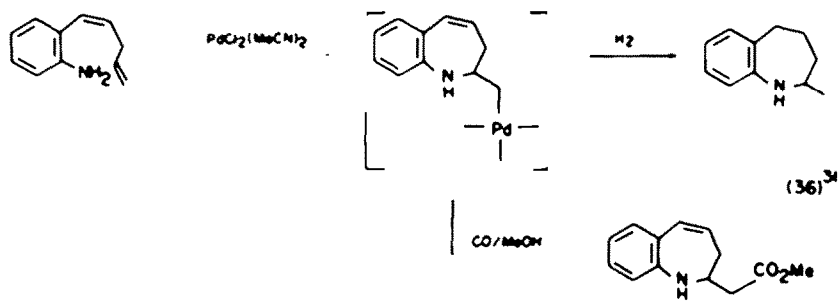


(34)

(35)

A number of other olefinic amines and amides cyclize in the presence of palladium(II) complexes. Although, as reported, most of these systems are *not* catalytic, it certainly should be possible to make them so.



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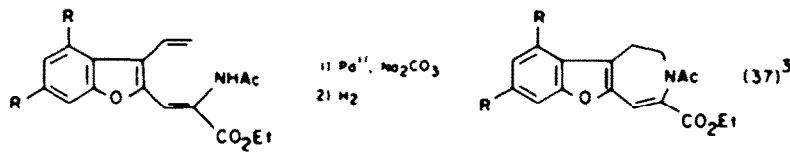

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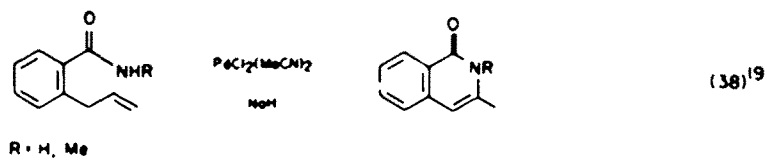
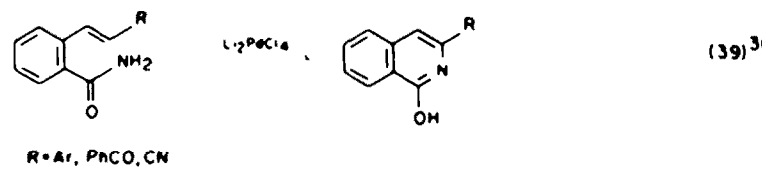


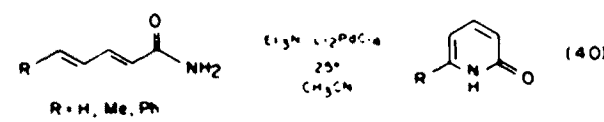
R = H, Me

(38)[19]



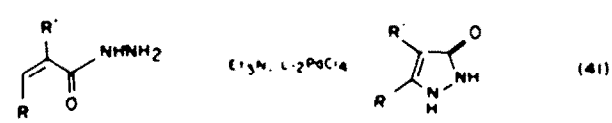
R = Ar, PhCO, CN

(39)[36]

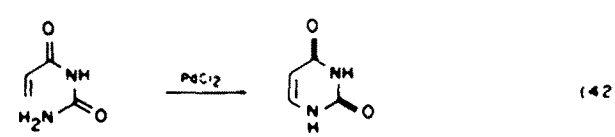


R = H, Me, Ph

(40)[37]



(41)[38]

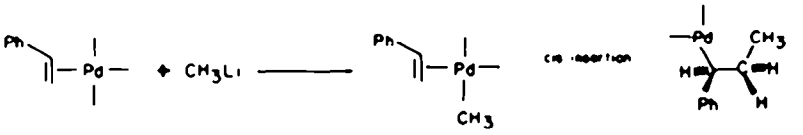


(42)[39]

Reactions of carbon nucleophiles with π-olefinpalladium(II) complexes

The use of carbanions as nucleophiles poses yet another set of problems. Carbanions are easily oxidized and palladium(II) is a reasonably strong oxidizing agent. Thus the major reaction of carbanions with π-olefinpalladium(II) complexes is reduction of the palladium(II) to metallic palladium with concommitant oxidative coupling of the carbanion. The facility of this undesired process is a function of the ease of reduction of the palladium(II) species, which, in turn depends

on the particular ligands associated with the metal. This phenomenon is seen in the reactions of methyllithium with styrene in the presence of palladium(II) salts. With palladium(II) chloride, only a 3% yield of β-methylstyrene is obtained, whereas with palladium(II) acetate, a 75% yield results, and with palladium(II) acetylacetonate a 90% yield results.[40] This increase in yield parallels an increase in the resistence of the palladium(II) salt to reduction. This alkylation proceeds by initial alkylation of the metal followed by a *cis* insertion of the olefin into the metal-carbon bond, followed by a *cis* β-hydride elimination (eqn 43). The regiochemistry of this alkylation, attack at the *less*



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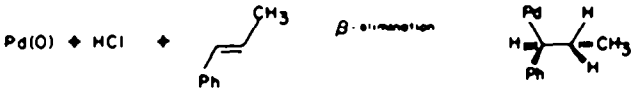
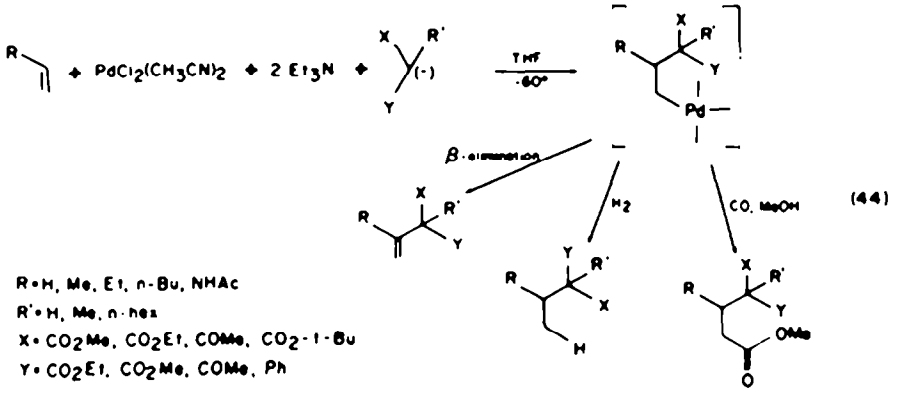


substituted carbon, is also consistent with this mechanism. This alkylation is restricted to methyllithium as the carbanion. Neither this process, nor the ones discussed below are catalytic processes, because of the inability of finding an oxidizing agent suitable to carry the requisite palladium(O) to palladium(II) redox chemistry and at the same time compatible with the carbanions used.

A considerably more general alkylation of olefins by carbanions has been developed based on observations of the related amination of olefins discussed above. In that reaction nucleophilic attack (amination) occurred on an olefinpalladium(II) *amine* complex, not on the corresponding chloride complex, suggesting that the reaction was quite sensitive to the ligands bound to the olefinpalladium(II) species. Similarly, reaction of olefinpalladium(II) *chloride* complexes with stabilized carbanions results in *no* alkylation of the olefin. However addition of two equivalents of triethylamine to the olefinpalladium(II) complex *prior* to addition of the carbanion leads to high yields of alkylation, with a range of stabilized carbanions and olefins (eqn 44).[41] Terminal

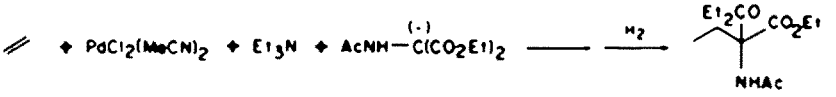


(44)

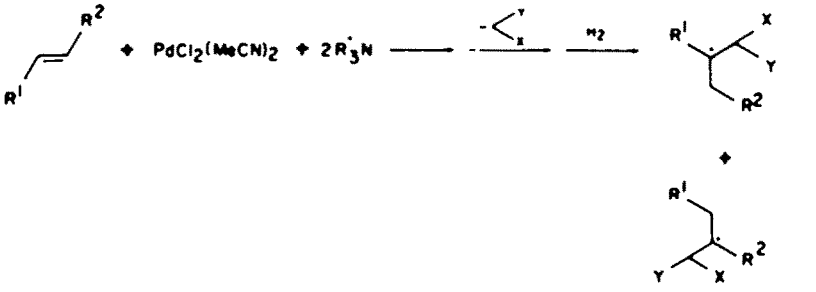
mono-olefins are alkylated in almost quantitative yield, with alkylation at the most substituted terminus predominating. (This regiochemistry is consistent with external, *trans* nucleophilic attack.) Electron-rich olefins such as enamides react in high yield, but electron-poor olefins such as acrylates do not alkylate at all. Internal olefins alkylate in only 30–40% yield, while isobutene and

cyclohexene do not react under these conditions. As expected, exposure of the unstable σ-alkylpalladium intermediate to carbon monoxide results in an overall "carboacylation" of the initial olefin.[42]

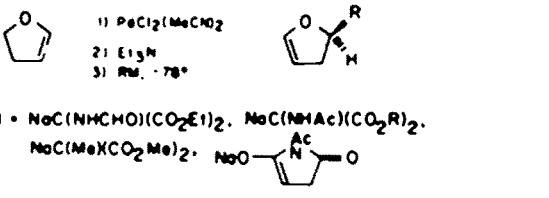
With α-acetamidomalonic esters as nucleophiles, α-aminoacid derivatives can be prepared (eqn 45).[43] By using internal olefins and chiral tertiary amines as ligands modest yields of alkylation product with up to 32% ee can be obtained (eqn 46).[44] Dihydrofuran alkylates cleanly α to the oxygen to give fair to good yields of α-alkylated dihydrofurans (eqn 47).[45]



(45)



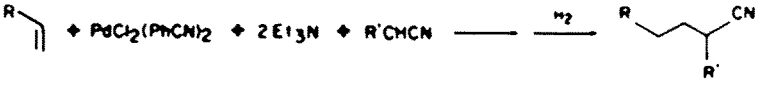
(46)



(47)

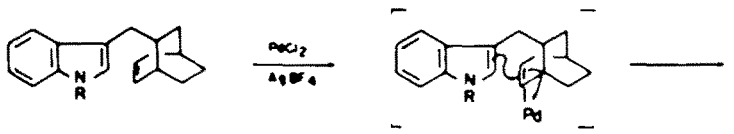
This reaction is restricted to the use of stabilized carbanions (pK_a 10–18) as nucleophiles. With less-stabilized carbanions reduction of the complexes without alkylation results. However, addition of HMPA [$(Me_2N)_3PO$] to the olefinpalladium(II) complex prior to addition of the triethylamine and the carbanion permits the use of much less stabilized carbanions [41] (another indication of the sensitivity of this reaction to the ligand environment). Under these conditions ketone and ester enolates, oxazoline anions (carboxylic acid anion equivalents), protected cyanohydrin anions (acyl anion equivalents) and even benzylmagnesium chloride, alkylate olefins in fair to excellent yields. Although somewhat dependent on the nature of the olefin and the anion, alkylation occurs predominately at the *less*-substituted position of the olefin, suggesting a change in mechanism from external nucleophilic attack (eqn 44) to attack at the metal followed by insertion (eqn 43). (With very reactive ($PhCH_2Li$) carbanions alkylation occurs *exclusively* at the less substituted position of the olefin.)

The source of palladium(II) in the above reaction is $PdCl_2(CH_3CN)_2$. When phenyllithium is used as the carbanion, the major product obtained is that from attack of $-CH_2CN$ on the olefin, rather than phenyllithium. Apparently, rapid proton transfer between the nitrile and the phenyllithium occurs, generating the nitrile anion, which then alkylates the olefin (eqn 48).[46] Externally generated nitrile anions react in a similar fashion. In all cases alkylation occurs at the less substituted terminus of the olefin to produce linear nitriles in fair to excellent yield.

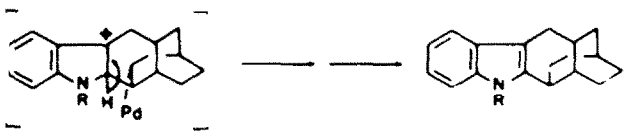


(48)

Two intramolecular alkylation reactions, both requiring stoichiometric amounts of palladium and both having uncertain mechanisms have recently been developed. The first involves the reaction of the indole-2-position with pendant olefins in the presence of palladium(II) chloride and silver(I) tetrafluoroborate.[47] The reaction is quite sensitive to the position of the olefin and may involve "electrophilic aromatic substitution" of the complexed olefin (highly electrophilic because of its formal cationic nature) on the indole-2-position. These results are summarized in eqns (49)–(52).



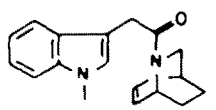
(49)



(50)

(low yield)

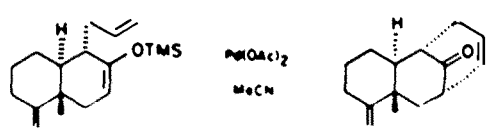
(51)



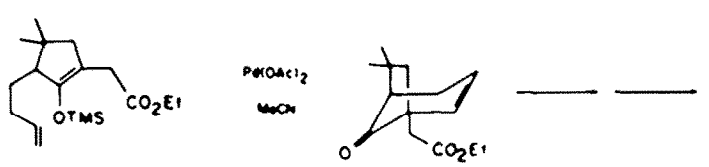
No cyclization

(52)

The second involves the cyclization of olefinic ketone trimethylsilylenol ethers in the presence of stoichiometric amounts of palladium(II) acetate (eqn 53).[48] Originally this reaction was thought to proceed via a π-oxyllalpalladium species, but it seems more likely that it involves nucleophilic attack of the enol ether on an olefinpalladium(II) complex. This is a rather general process and numerous examples have been reported.[49] This chemistry has been used to synthesize quadrone (eqn 54).[50]



(53)

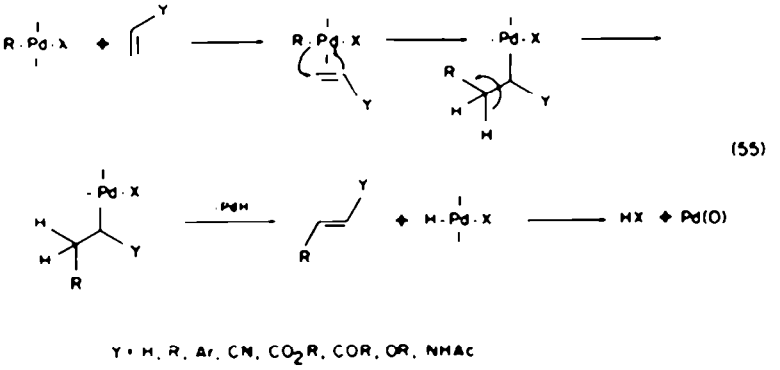


(54)

Insertion reactions of olefins with σ-alkylpalladium(II) complexes

In the above discussion, it was seen that σ-alkylpalladium(II) complexes (from nucleophilic attack on π-olefinpalladium(II) complexes) "inserted" olefins to form new carbon–carbon bonds. This insertion reaction is general for σ-alkylpalladium(II) species, regardless of their genesis, and is the second synthetically important class of reactions involving mono-olefin complexes of palladium(II) to be dealt with in this review.

A considerable amount is known about this insertion process. It is thought to involve; (1) coordination of the olefin to the alkylpalladium(II) species in a position *cis* to the alkyl group; (2) a *cis* insertion (migration of the alkyl group from the metal to the olefin) of the olefin into the metal–carbon σ-bond; (3) rotation about the former olefinic bond; (4) a *cis* β-hydride elimination to regenerate the olefin double bond; (5) loss of HX to produce a palladium(O) species. These steps are summarized in eqn (55).



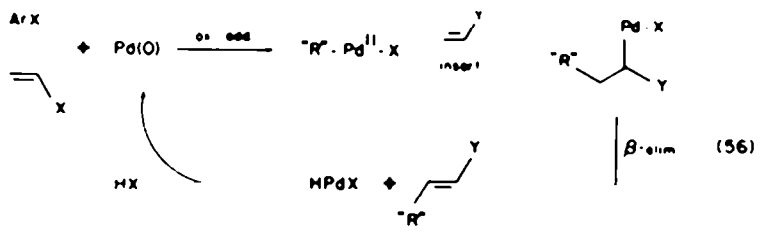
(55)

Y = H, R, Ar, CN, CO_2R, COR, OR, NHAc

Most types of olefins undergo this insertion process, and regardless of the electronic nature of the olefin, insertion occurs to place the R group on the less-substituted terminus of the olefin, implying steric rather than electronic control of regiochemistry. (When the insertion is an intramolecular process, the regiochemistry is less predictable because of difficulty in assessing the various strains resulting from ring formation). A major limitation of insertion chemistry is that, almost invariably, the R group *must not* have β-hydrogens, since β-hydride elimination is usually easier than insertion. Thus, in practice, this insertion chemistry is limited to σ-aryl and σ-vinylpalladium(II) species. The requisite σ-alkylpalladium(II) species are available from both oxidative addition of organic halides to palladium(O) complexes and by transmetallation processes. Both of these approaches are discussed below. In addition "ortho-palladation" processes will be briefly mentioned.

Insertion processes involving oxidative addition

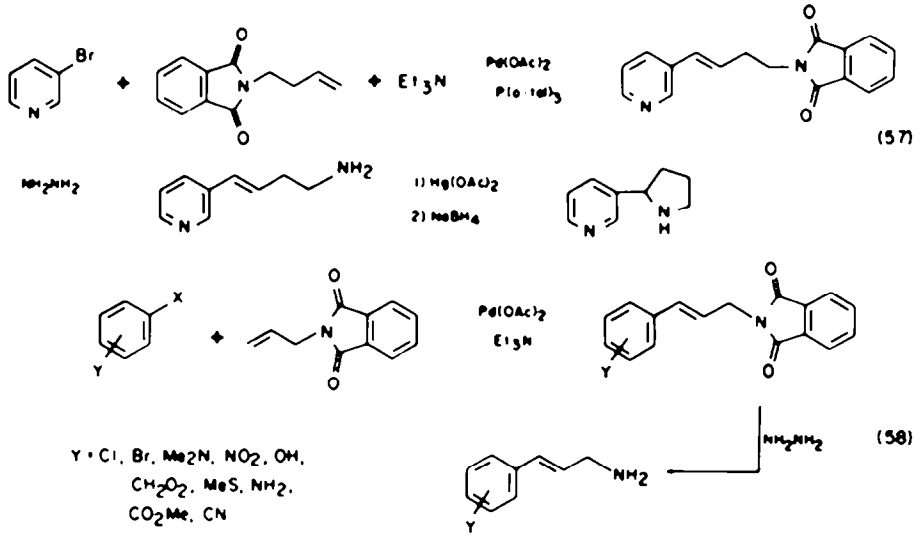
Aryl and vinyl halides react with palladium(O) complexes in an "oxidative addition" process, forming aryl- or vinylpalladium(II) complexes. When this reaction is carried out in the presence of an olefin, insertion occurs to form new unsaturated products and to regenerate the palladium(O) species, making the entire process catalytic (eqn 56). This is a very well established and extensively



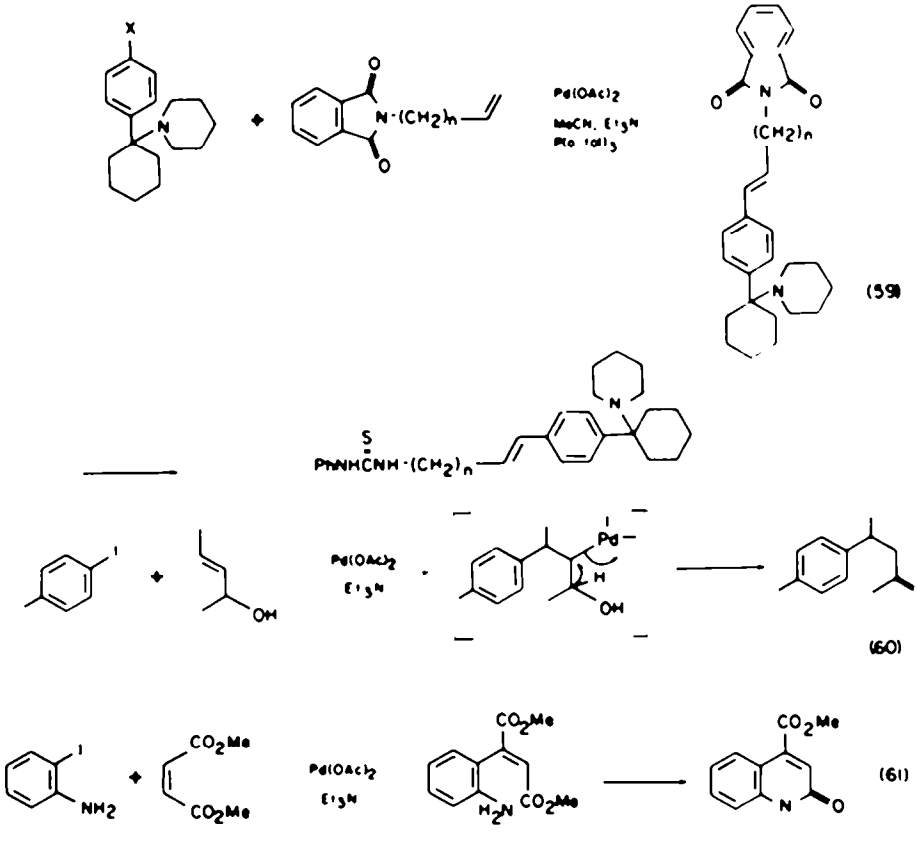
(56)

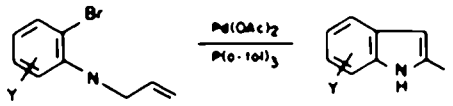
studied process, and is the subject of several recent reviews.[51] Hence, only recent, synthetically interesting, examples of this chemistry will be presented. (To prevent confusion, note that although this chemistry clearly involves palladium(0) species as catalysts, most reactions start with palladium(II) salts as the catalyst precursor. *In situ* reduction to palladium(0) is assumed and must occur.)

With 3-bromopyridine as the aryl halide and N-3-butenylphthalimide as the olefin, nornicotine was synthesized (eqn 57).[52] A wide variety of σ-aryl allyl amines is available using aryl halides and N-allylphthalimide (eqn 58).[53] Very similar chemistry was used to synthesize amino-



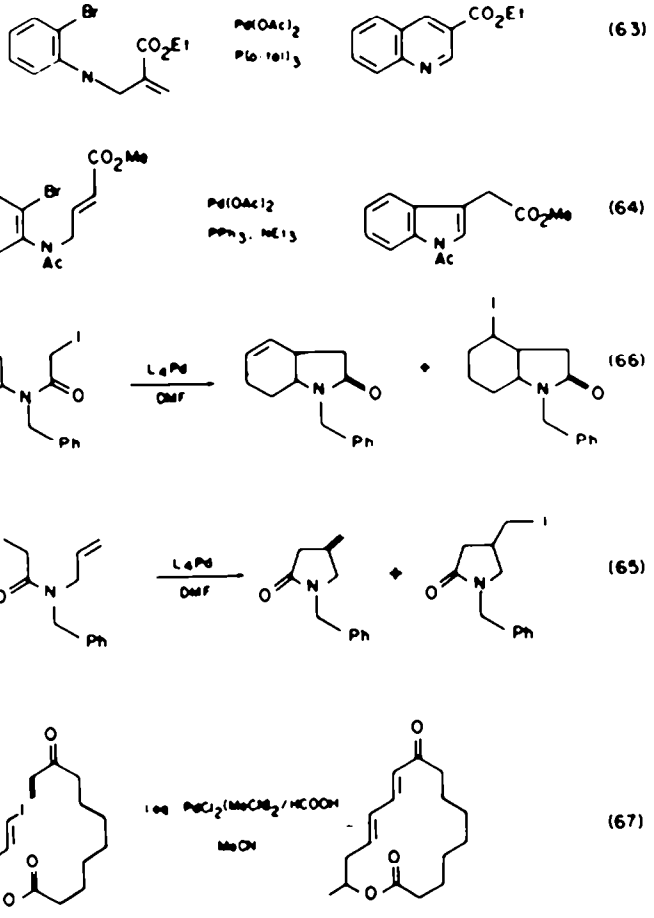
alkylphencyclidines (eqn 59).[54] With allyl alcohols as the olefin component, ketones are produced (eqn 60).[55] 2-Quinolones result from iodoanilines and maleate esters (eqn 61).[56]





(62)

Intramolecular versions of this process are particularly useful for making heterocyclic compounds. Indoles result from o-halo-N-allylanilines (eqn 62).[57] Note that the regiochemistry of this cyclization is different from most intermolecular reactions. Depending on substitution, however, six membered ring formation may also be observed (eqn 63). Indoleacetic acid is formed in a similar manner (eqn 64).[58] Lactams are formed in modest yield by the cyclization of olefinic α-haloamides (eqns 65 and 66).[59] All of these reactions require only catalytic amounts of palladium. In contrast cyclization to form the macrocyclic lactone shown in eqn (67) requires stoichiometric amounts of palladium(II) halide under reducing conditions.[60]



(63)

(64)

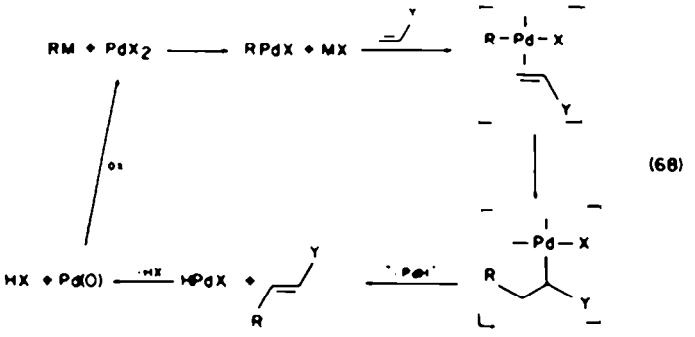
(66)

(65)

(67)

Insertion processes involving transmetallation

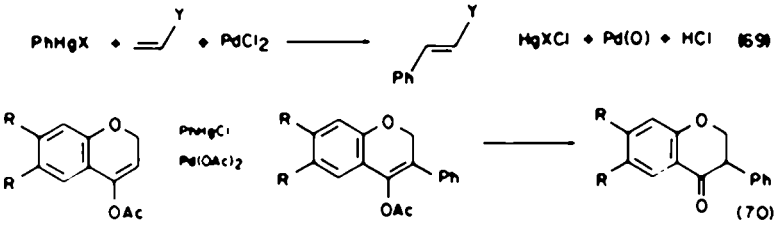
A number of covalent, main-group organometallic species react with palladium(II) halides to transfer the organic group from the main group metal to the palladium (transmetallation) generating a σ-alkylpalladium(II) species. The most commonly used main group metals are mercury and tin, although aluminum, boron, thallium, zinc and zirconium are used, although to a lesser extent. Again, because of the facility of the β-hydride elimination process for organopalladium species, the organic group used must lack β-hydrogens, thus, in practice, limiting transmetallation reactions to aryl or vinyl groups. When transmetallation to palladium is carried out in the presence of an olefin, insertion occurs, forming a new carbon–carbon bond (eqn 68).



(68)

In transmetallation processes palladium(II) species are required for the initial step, but palladium(O) species are produced in the final step. Thus an oxidizing agent is required to make these transmetallation-insertion processes catalytic in palladium.

Arylmercuric halides are extensively used in transmetallation processes, primarily because many of them are available by direct mercuration of the aromatic compound. One of the earliest manifestations of the "Heck" arylation of olefins involved phenylmercuric chloride and activated olefins (eqn 69).[61] Isoflavones can be prepared by the arylation of appropriate enol ethers (eqn 70).[62]

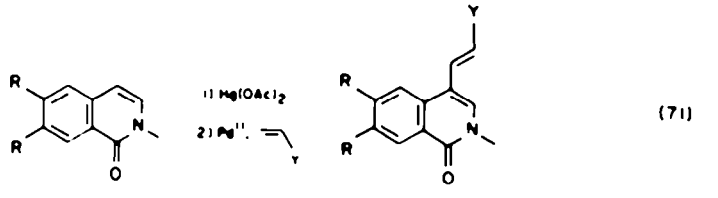


(69)

(70)

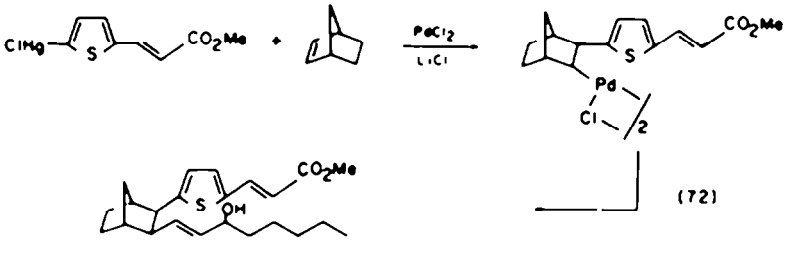
Isoquinolones undergo direct mercuration at the 4-position, permitting facile introduction of olefinic side chains at that position (eqn 71).[63] By using mercurated thiophenes and norbornenes, bicyclic prostaglandin derivatives are available (eqn 72).[64] None of these reactions has been carried out catalytically, although in principle this should be possible.

This reaction has found extensive application in nucleoside chemistry because direct mercuration of pyrimidines is quite easy,[65] and transmetallation-insertion processes proceed well. This chemistry is summarized in eqn (73).

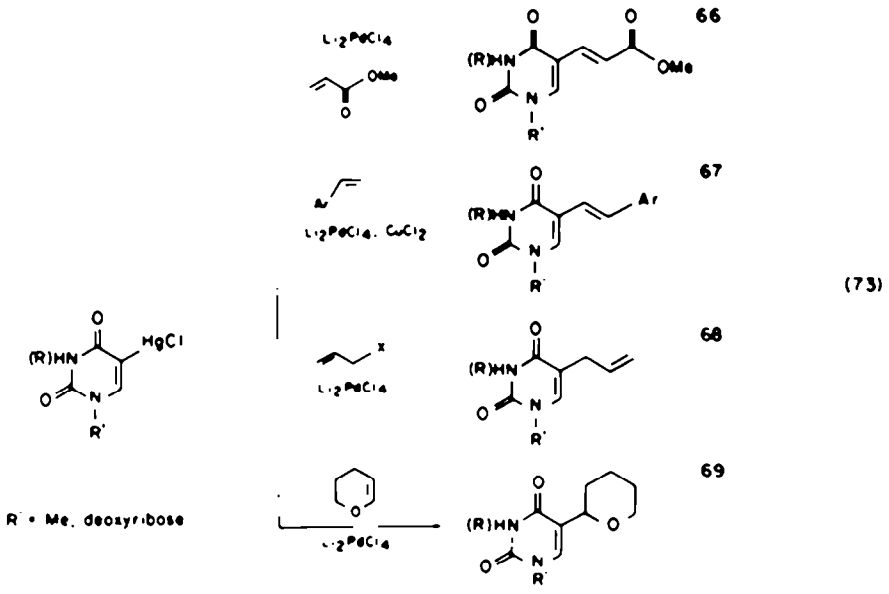


(71)

Y = CO Me, Ph, p-ClPh, o-ClPh

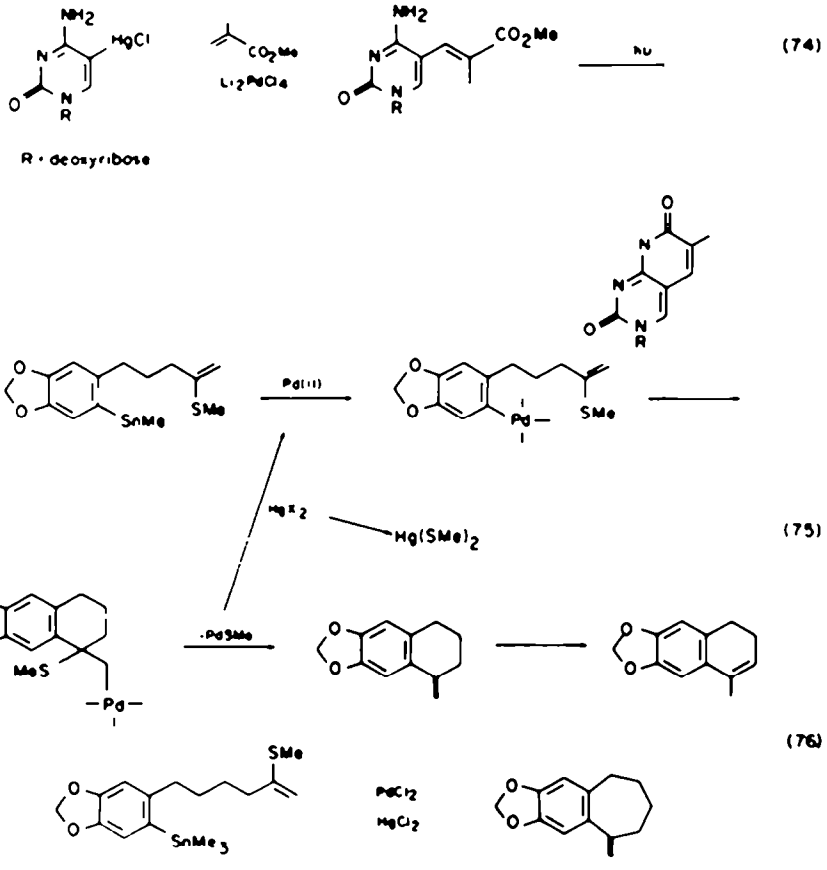


(72)



Bicyclic material can be made this way (eqn 74),[70] and mercurated purines undergo analogous reactions.[69a] At least some of these reactions have been run in a catalytic fashion, and again, in principle, they all should be.

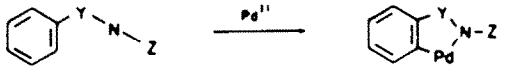
Organotin complexes also readily transmetallate to palladium(II) compounds, making these main group organometallics versatile sources of organic groups for use in organopalladium(II) chemistry. To date little use of organotin compounds in olefin insertion chemistry has been made. A very nice intramolecular reaction of this type is seen in eqns (75) and (76), in which a vinyl sulfide



is the inserting olefin.[71] This system is catalytic in palladium only when mercury(II) salts are added to scavange the thiol released upon elimination. In the absence of added mercury, the sulfur compounds rapidly poison the palladium catalyst.

Insertion processes involving "ortho-palladation"

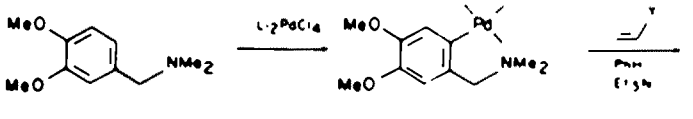
Aromatic compounds containing nitrogen in a benzylic position react with palladium(II) compounds to undergo a ligand directed "ortho-palladation", introducing the palladium ortho to the ligand in an electrophilic aromatic substitution reaction.[72] The chemical nature of the nitrogen is of minor importance, as long as it has a lone pair of electrons with which to coordinate the metal (eqn 77). This ortho-palladation generates a σ-arylpalladium(II) complex, which should and does

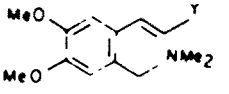


(77)

YNZ = CH_2NMe_2, 2-Py, CH=NR, $CH_2N=CR_2$, NHN=CHR, CH=NOH, $CH=NNR_2$

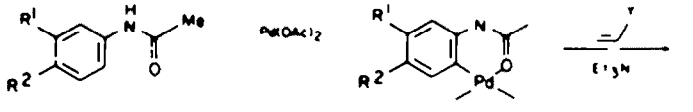
insert olefins. For example the palladium complex from a substituted dimethylbenzylamine inserts a variety of olefins in fair to good yield (eqn 78).[73] Acetamides also "ortho-palladate", somewhat of a surprise since in this case oxygen is the coordinating ligand and a six (not a five) membered ring is formed. Nonetheless, these complexes also readily insert olefins in quite good yield (eqn 79).[74]





(78)

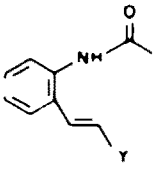
Y = COMe, CO_2Et, Ph, Ar



R^1 = H, Me, OMe, Cl, CO_2Et, COMe

R^2 = H, Me, OMe, Cl, CO_2Me

(79)



Y = Ar, CN, $CH(OEt)_2$, COMe, CO_2Me, OAc, H

The major problem with this chemistry, from a synthetic point of view, is that nobody has managed to devise a catalytic system, and it is not at all clear how to do this. The difficulty is that the conditions required for insertion (addition of Et_3N and heating) are incompatible with the conditions for ortho-palladation. Thus the two steps must be carried out individually and sequentially. A solution to this problem would be a major advance in this area, and is an area of research that warrants substantial effort.

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