

Transition-metal-catalyzed reactions of carbon–heteroatom bond formation by substitution and addition processes*

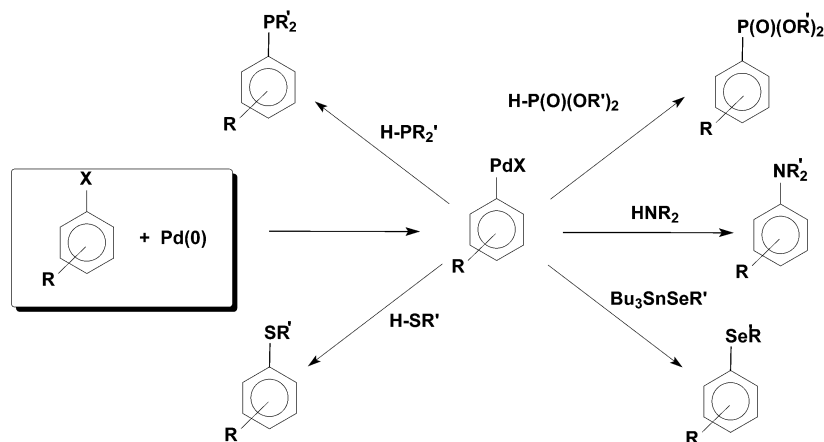
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Abstract: Two types of transition-metal-catalyzed cross-coupling reactions, which both lead to the formation of carbon–heteroatom bonds, are considered: $RX + E-H$ and $E-X + RM$. The potential of addition reactions of $E-H$ or $E-E$ to double or triple bond in $C-E$ bond formation is also demonstrated.

Keywords: Transition-metal-catalyzed reactions; homogeneous catalysts; carbon–carbon; carbon–heteroatom; bond formation; Ullmann reaction.

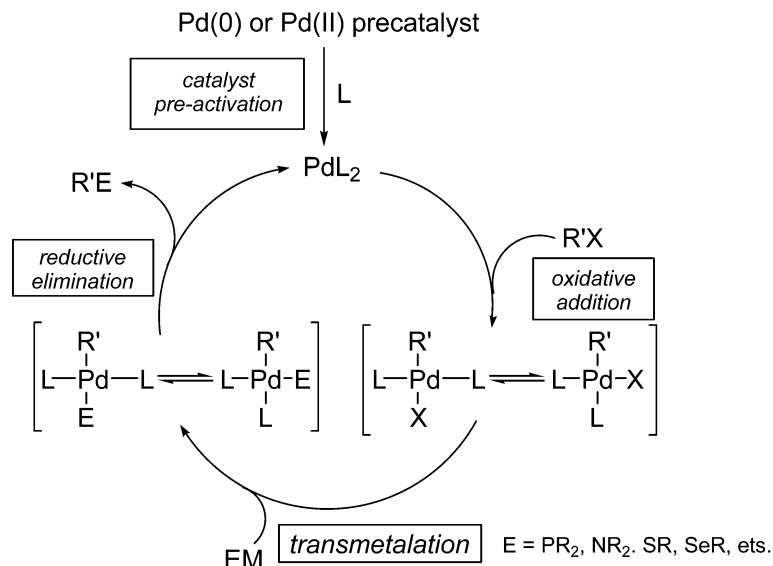
The application of transition-metal complexes as homogeneous catalysts has led to the development of simple and efficient methods of carbon–carbon and carbon–heteroatom bond formation. Among the complexes used for this purpose, the complexes of palladium occupy a special place [1], but besides, the nickel complexes are also utilized, and in recent years the soluble copper complexes are used increasingly [2] under conditions much more mild than in Ullmann reactions. Reactions leading to the formation of $C-P$, $C-N$, $C-Se$, $C-S$, and similar bonds involve a heteroanion analog of an organometallic compound in the cross-coupling process (Scheme 1).



Scheme 1 Pd-catalyzed reactions.

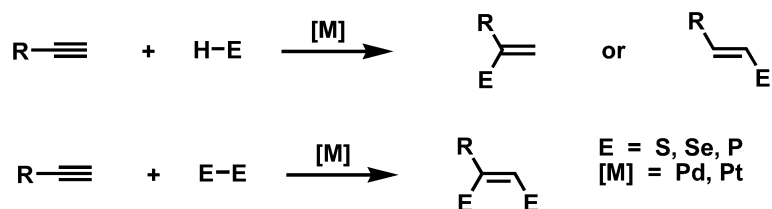
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Following the analogy with the classical catalytic cycle of cross-coupling, one can write a cycle with a heteroanion taking part in the transmetalation step (Scheme 2). However, this would be a superficial treatment, since in many reactions, such as the reactions with trialkylphosphites or amines, the anion is not formed, and the mechanism has to be essentially different.



Scheme 2 The catalytic cycle for Pd-catalyzed cross-coupling reactions.

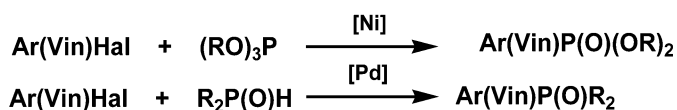
Another catalytic pathway of carbon–heteroatom bond formation is based upon the addition reactions of E–H and E–E bonds to unsaturated compounds—alkynes, alkenes, carbonyl compounds, imines. From the “atom efficiency” viewpoint, these reactions are more attractive than the substitution reactions. Various terminal alkynes can be used in the reaction with H–E and E–E bonds (Scheme 3) [3].



Scheme 3 The addition reactions of H–E and E–E bonds to triple bond.

FORMATION OF CARBON–PHOSPHORUS BOND

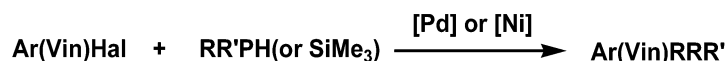
Aryl- and vinylphosphonates can be obtained by the reaction of aryl- or vinylhalides with trialkylphosphites with catalysis by palladium or nickel complexes. Yet the conditions required for this reaction are rather harsh. Alternatively, the same phosphonates may be successfully obtained by the cross-coupling with dialkylphosphites, which may be carried out using a variety of different reaction conditions: phase-transfer catalysis, aqueous solvents, neat water, and even without solvent; with palladium and nickel complexes as catalysts [4].



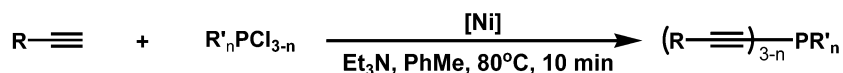
Tertiary phosphines are formed in the cross-coupling reaction of aryl halides with free secondary phosphines or their Si-derivatives. The latter modification also allows one to obtain secondary phosphines.

Today, this reaction is widely used in the synthesis of new ligands.

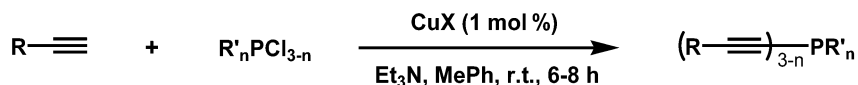
Cross-coupling reactions with phosphines are also catalyzed by nickel complexes, which is shown on the example of various α - and β -substituted vinyl halides.



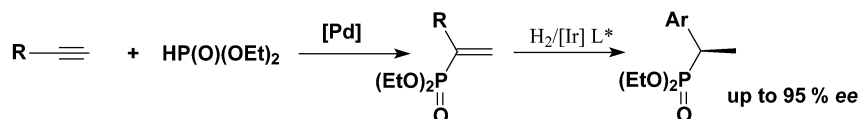
The alkynyl phosphorous derivatives can be obtained through the reaction of $\text{R}_n\text{PCl}_{3-n}$ with terminal alkynes catalyzed by nickel complexes [5]. Reaction may be viewed upon as a heteroanalog of Sonogashira reaction.



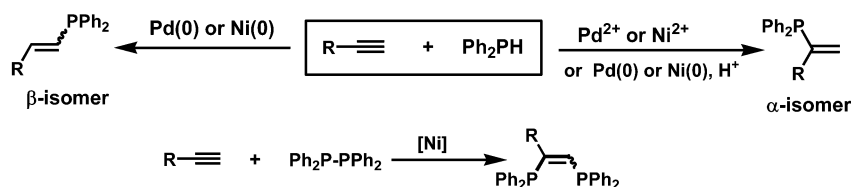
The Cu(I) complexes are equally capable of catalyzing this reaction, in which case it may be performed at room temperature even with such a weak electrophile as $(\text{RO})_2\text{PCl}$ [6]. Reaction may be viewed as a catalytic form of a heteroanalogous Castro reaction.



The palladium-catalyzed addition reaction of dialkylphosphites to terminal alkynes results in vinylphosphonates, which may be reduced to give a very important class of phosphorous derivatives, including those in an optically active state, such as P-analogs of naproxen and ibuprofen [7,8].

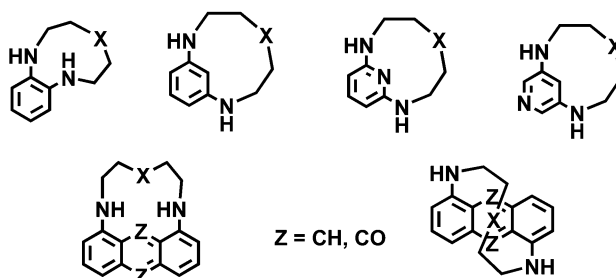


Nickel complexes have turned out to be more active in catalyzing the addition of diphenylphosphine and tetraphenyldiphosphine to alkynes and Ph_2PH to styrenes [9] and alkenylalkyl ethers [10]. The regioselectivity of addition can be controlled by changing the actual catalytic complex [11].

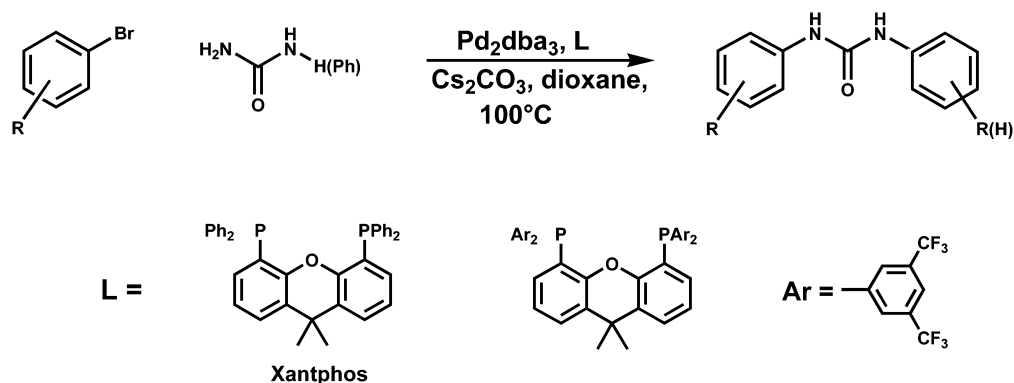


FORMATION OF CARBON–NITROGEN BOND

We have carried out an extensive series of studies on the arylation of various polyamines and have found conditions allowing for selective mono-, di- and tetraarylation [12]. In the case of dihaloarenes, one or two amino-groups can be introduced, and in the reactions with polyamines a new family of polyaza-cycles was obtained [13]. Reactions of this kind were carried out for ortho- and meta-dihalobenzenes, α,α' - and β,β' -dihalopyridines as well as for 1,8- and 1,5-dihaloanthracenes and anthraquinones.



To obtain biologically active compounds, the arylation of urea with various aryl halides, using Xantphos and its modified derivative as ligands, was performed [14].

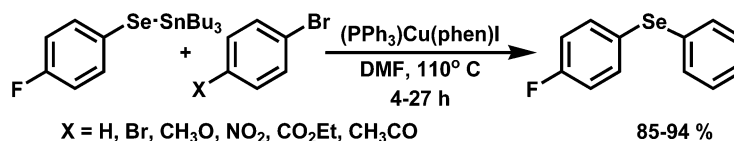


Using these ligands, and also 2-[di-(*tert*-butyl)phosphino]biphenyl, we have also managed to carry out the amination and amidation of bromindoles, bromotetrahydrocarbazolones, and bromotetrahydropyrazinocarbazoles. Certain of these amination and amidation reactions were carried out without solvent, giving almost the same yields as in solution [15].

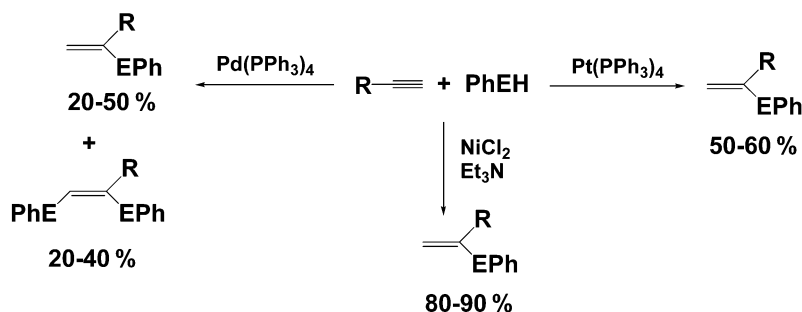


FORMATION OF CARBON–SELENIUM AND CARBON–SULFUR BONDS

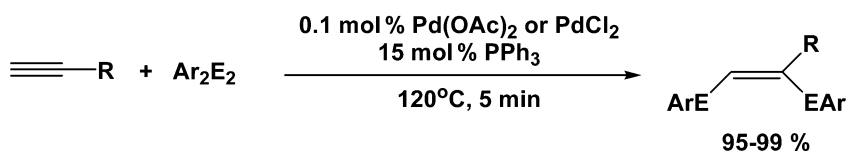
The synthesis of diarylselenides by Pd-catalyzed reaction was performed using ArSeSnBu_3 and aryl iodides, or in case of Ni-catalyzed reaction, aryl triflates [16]. Yet, with both catalysts one cannot use aryl bromides, since instead of cross-coupling a much faster disproportionation of the starting tin selenide takes place. However, reaction with aryl bromides was successful with Cu(I) complexes [17].



Formation of vinylselenides and vinylsulfides may be also performed by the transition-metal-catalyzed addition of selenols and thiols (ArSeH and ArSH) to terminal alkynes. Best results in this reaction are achieved by the use of platinum, and especially nickel complexes, because with palladium complexes a side process, leading to diselenides and disulfides and their addition to alkyne, is observed. It is noteworthy that the addition of ArEH ($\text{E} = \text{Se, S}$) leads to Markovnikov isomer, exclusively [18].



The addition of A_2E_2 is better catalyzed by palladium complexes and proceeds stereoselectively as *syn*-addition [19].

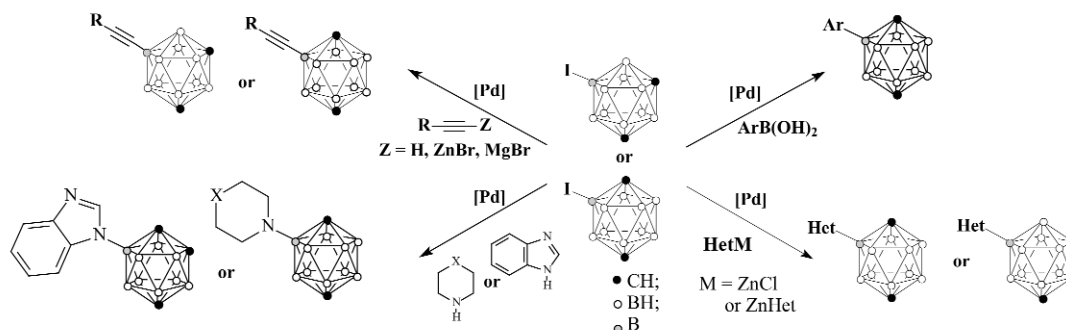


In the course of the work, we have solved a number of structures of intermediate complexes and reaction products. These reactions can be also carried out without solvent in an excess of phosphine [20]. In that case, raising the temperature to 120 °C allows one to use extremely low catalyst loadings and reduce the reaction time to several minutes. The feasibility of recycling the catalyst without loss of its catalytic activity was also demonstrated.

FORMATION OF BORON–CARBON AND BORON–NITROGEN BONDS

The task of attaching aryl- and hetaryl fragments to the boron atom in carborane molecules required the activation of boron–iodine bond in the molecules of 9-iodocarboranes. A careful choice of ligands

in the palladium complexes allowed us to carry out reactions with arylboronic acids [21], organozinc and -magnesium compounds, various terminal alkynes [22], as well as certain amines and azoles (Scheme 4).



Scheme 4 Reactions of 9-iodocarboranes with organometallic compounds, alkynes, and amines.

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