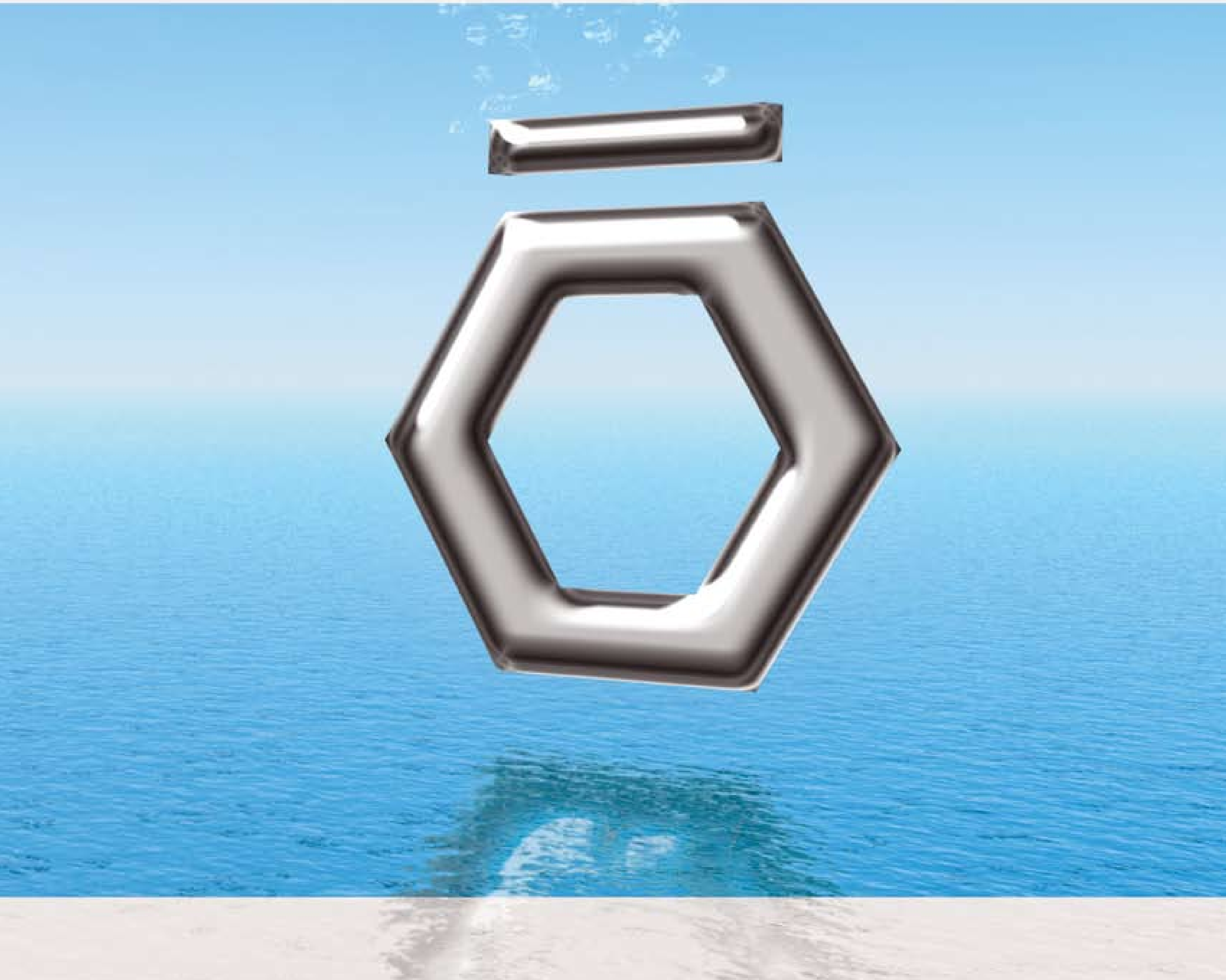
METAL CATALYSTS



ACROS
ORGANICS

CONTENTS

COUPLING REACTIONS WITH CATALYSTS AND REAGENTS FROM ACROS ORGANICS

INTRODUCTION

Precious metal catalysis is booming in organic synthesis since the last decades and many precious metal compounds have been synthesized to fulfil the need for specialized catalysts[1].

Some prominent examples for modern catalytical reactions are:

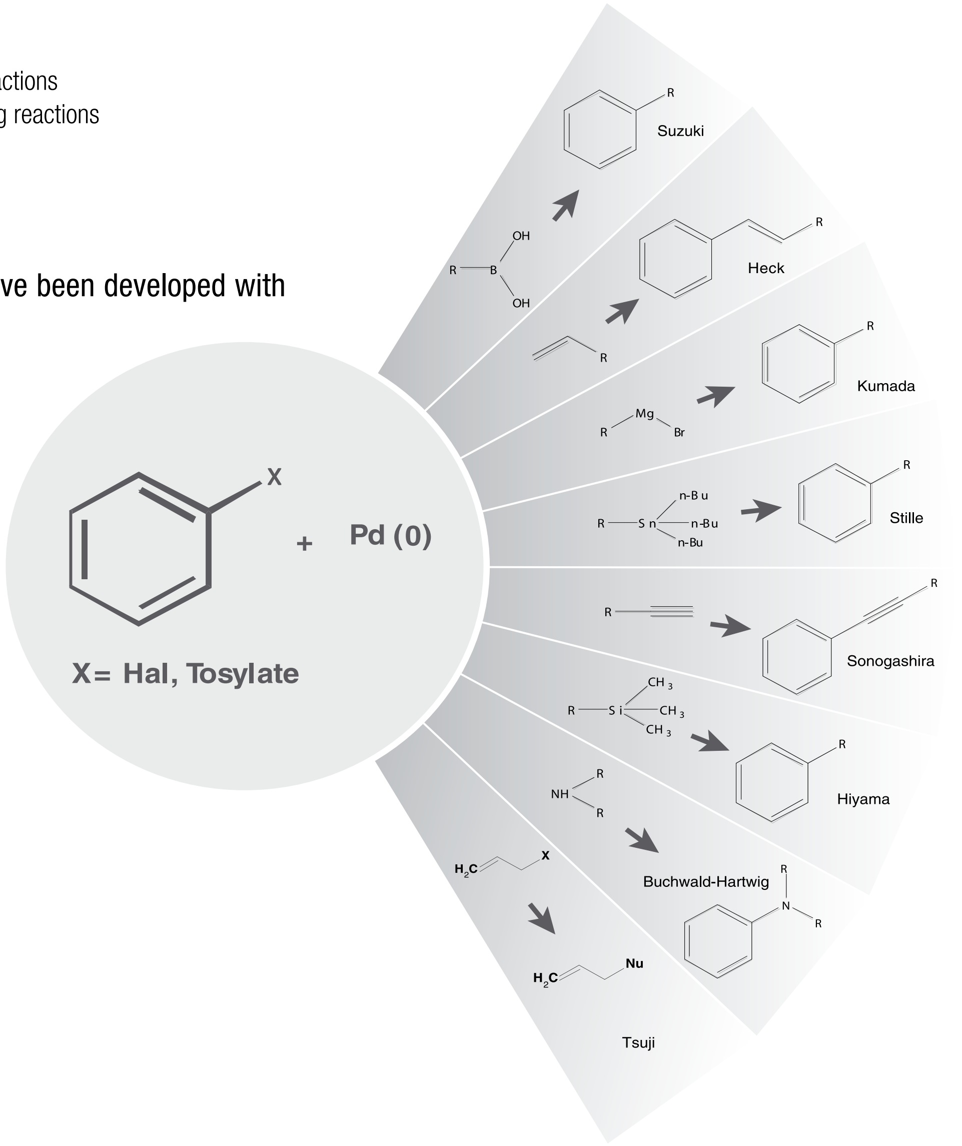
- › Hydrosilylations
- › Carbonylations and decarbonylations
- › Asymmetric hydrogenations
- › Selective oxidations
- › Alkene-methatesis
- › Carbon-Carbon-coupling reactions
- › Carbon-Heteroatom-coupling reactions

Especially the precious-metal catalysed coupling reactions have remarkably enlarged the toolbox of organic chemistry since their first examples in the late 1960th.

A broad variety of substrates and possible targets, good tolerance of different functional groups, mild reaction conditions, high yields and efficient catalysts make these modern couplings to widely used reactions.

Several coupling reactions have been developed with different substrates:

- › Heck
- › Stille
- › Suzuki
- › Sonogashira
- › Kumada
- › Negishi
- › Buchwald-Hartwig
- › Hiyama
- › Tsuji



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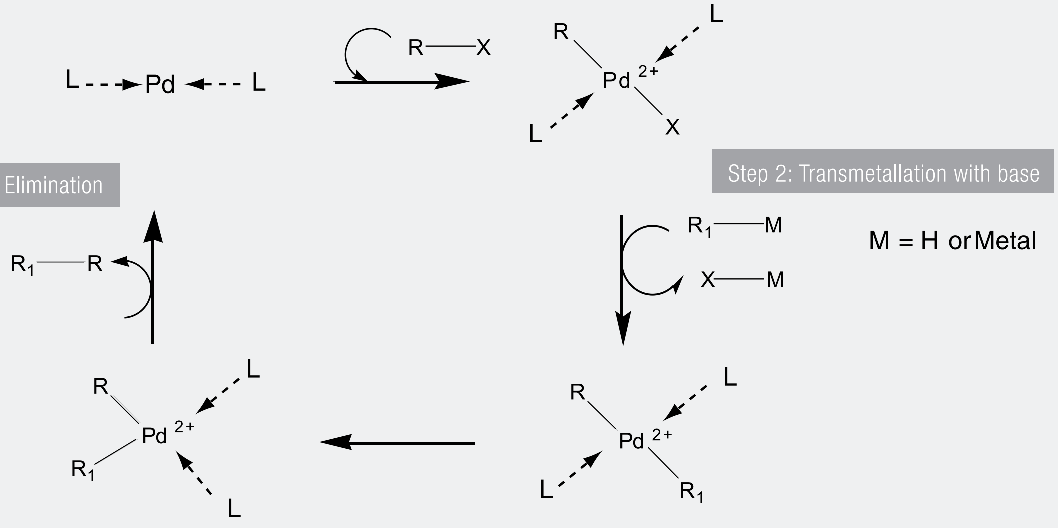
[1] P.B.Kettler, Organic Process Research & Development 7 2003 342

Most of these coupling reactions have a similar catalytical cycle:

Step 1: Oxidative Addition

The oxidative addition is the rate determining step. The reactivity of the halogenides follows the order $I \sim (OSO_2CF_3) > Br >> Cl$ in most coupling reactions

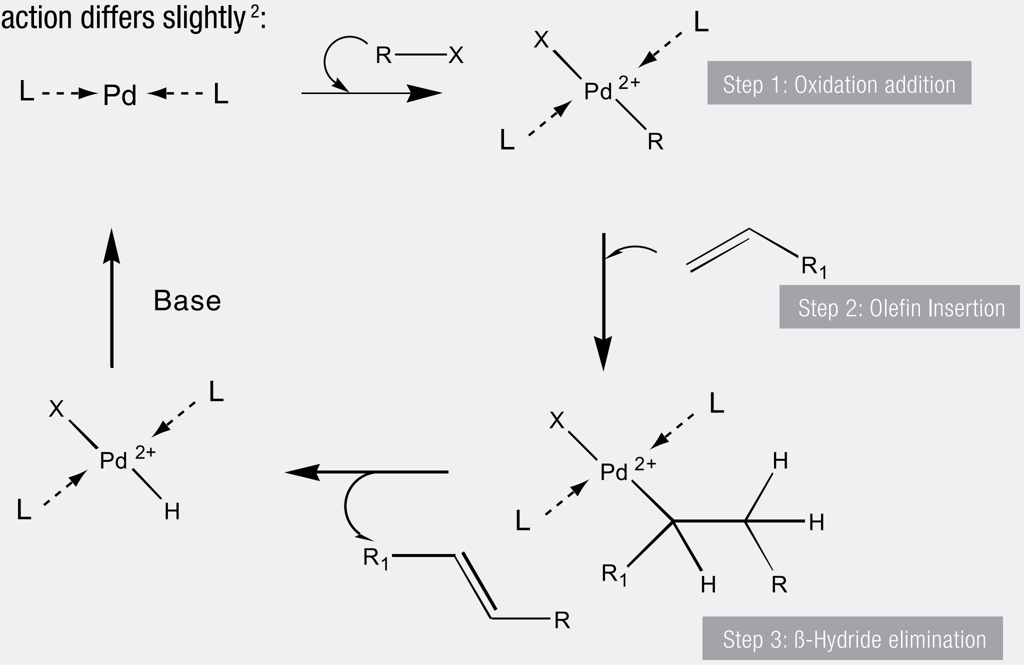


Step 2: Transmetallation with base

Step 4: Reductive Elimination

Step 3: *Cis-trans*-isomerisation

The Heck-reaction differs slightly[2]:



Step 1: Oxidation addition

Step 2: Olefin Insertion

Step 3: ß-Hydride elimination

The following pages give an overview over the most common carbon-carbon and carbon-heteroatom coupling reactions, the catalysts and the substrates offered by Acros Organics.

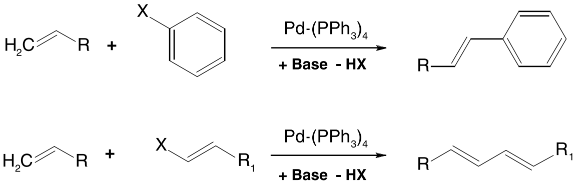
---

[2] Ch.Elschenbroich, A.Salzer, Organometallchemie, B.G.Teubner, Stuttgart 1988

HECK-REACTION[1]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (I)

The reaction was discovered in the end of the 1960th and has since then achieved the status of a standard-reaction in organic synthesis[2]. In the Heck-reaction an alkene (1) is coupled with a aryl- or alkenyl-halogenide (2) to vinylarenes or dienes (3) *(Scheme 1)*.

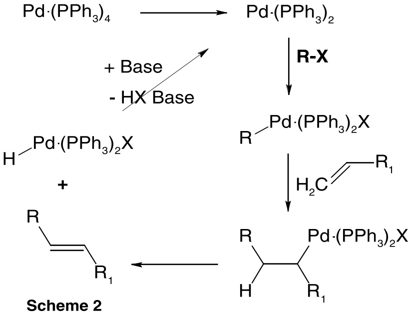


X = I, Br, (Cl), Triflate

Scheme 1

The reaction is catalysed by palladium(0)complexes with tertiary phosphine-ligands. The catalyst is either added directly, i.e. as tetrakistriphenylphosphine palladium(0) (Acros 20238) or, more common, the catalyst is produced in situ by reduction[3] of palladium-salts in the presence of a suitable phosphine-ligand.

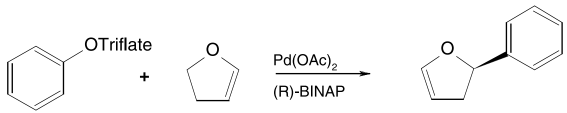
Because of the oxidative addition of R-X to the $Pd(PPh_3)_2$ *(Scheme 2)* the rate determining step is the reactivity of the halogenides (**ArI** > **ArBr** > **ArCl**).



Scheme 2

Terminal alkenes are good substrates for the Heck-reaction and react at the non-substituted carbon. Non-terminal, 1,2-disubstituted alkenes give usually product mixtures, with a preference for the less sterically hindered carbon[5].

The choice of the right amine-base[6] and especially the right phosphine-ligand has great influence on the selectivity and reactivity in the Heck-reaction.



Scheme 3

Chiral ligands like (R)- or (S)- Binap have been used for a enantioselective Heck-reaction *(Scheme 3)*[6,7,8].

USEFUL CHEMICALS FROM **ACROS ORGANICS** FOR THE HECK-REACTION

Tetrakis(triphenylphosphine)palladium(0) 99%	20238	1 g / 5 g	Bis(tri-t-butylphosphine)palladium(0) 98%	36350	100 mg
Palladium(II) acetate 47.5% Pd	19518	2 g / 10 g	Bis(tricyclohexylphosphine)palladium(0)	36351	100 mg
Palladium(II) chloride 59% Pd	19520	5 g	Tri-m-tolylphosphine 98%	31728	5g
Palladium(II) chloride 99,999%	36967	1 g / 5 g	Tri-p-tolylphosphine 95%	42233	5g
Bis(triphenylphosphine)palladium(II) chloride 15% Pd	19732	1 g / 5 g	Tri-o-tolylphosphine 99%	42232	5g
Bis(triphenylphosphine)palladium(II) chloride 98%	29925	250 mg / 5 g	Tris(4-methoxyphenyl)phosphine 95%	42224	10 g
Tris(dibenzylideneacetone)dipalladium(0) 97%	31877	500 mg / 5 g	Tris(4-chlorophenyl)phosphine 97%	42221	2 g
Bis(dibenzylideneacetone)palladium	29197	1 g / 5 g	Triisopropylphosphine 98%	31733	1 g / 5 g
Bis(triphenylphosphine)palladium(II) acetate 99%	20927	1 g / 5 g	Tri-tert-butylphosphine 95%	36098	1g / 5 g
(R)-(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 99+%	26553	250 mg	Trimesitylphosphine 97%	32113	1 g
(S)-(-)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 99+%	26554	250 mg	Tris(2,6-dimethoxyphenyl)phosphine	36496	5 g / 25 g
(±)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl	36864	5 g	Tricyclohexyl phosphine 97%	42161	5 g

Acros offers currently more than 160 Aryl iodides and over 550 Aryl bromides.

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---

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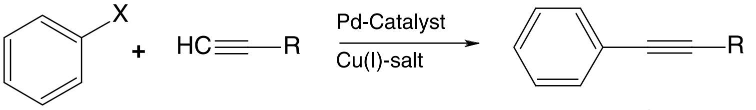
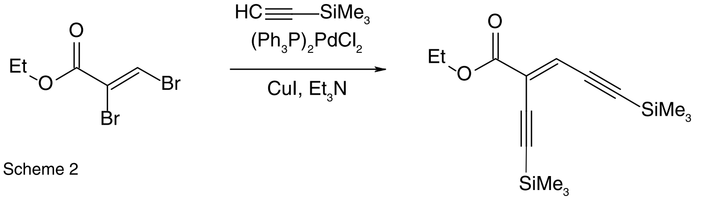
SONOGASHIRA-REACTION[1]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (II)

The Sonogashira-reaction and the closely related Stephens-Castro reaction[2] consists of the palladium-catalysed coupling of copper-acetylides and aryl-halogenides to yield alkynylarenes[3] (*Scheme 1*).



Scheme 1

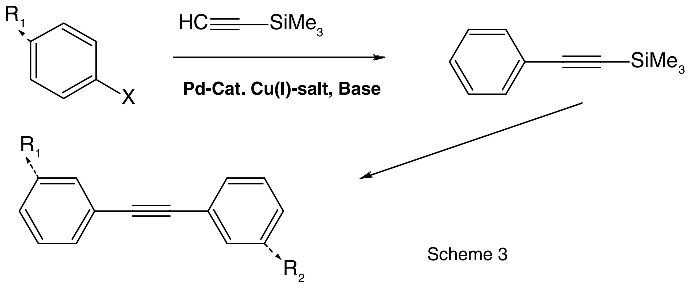


Scheme 2

The Sonogashira-reaction has a broad scope, tolerating several functional groups. It can be performed with ammonia as base in aqueous solution[8] and even works with palladium on carbon as catalyst[9] instead of homogeneous palladium catalysts. Recent improvements of the reaction are the development of efficient catalysts for the use of arylchlorides[10] and copper-free protocols[11].

This reaction is one of the most important reactions to produce alkenyl- and aryl-acetylenes[4], which have recently got a lot of attention as endiyn-antibiotics[5,6] (*Scheme 2*).

The use of silylated acetylene avoids the coupling at both positions, but if required, the silyl-protecting group can be removed in-situ, to enable the second coupling reaction i.e. for the synthesis of un-symmetric bis-arylethynes[7] (*Scheme 3*).



Scheme 3

CATALYSTS AND REAGENTS FROM **ACROS ORGANICS** FOR THE SONOGASHIRA-REACTION

(Triethylsilyl)acetylene	36873	1 g / 5 g	Bis(benzonitrile)palladium(II) chloride	20790	1 g
Trimethylsilylacetylene 98%	20357	5 g / 25 g	Bis(triphenylphosphine)palladium(II)chloride 98%	29925	2,5 g / 5 g
1-(Trimethylsilyl)-1-propyne 98%	22353	1 g / 5 g	Tetrakis(triphenylphosphine)palladium(0) 99%	20238	1 g / 5 g
1,4-Bis(trimethylsilyl)-1,3-butadiyne 98%	22539	5 g	Palladium(II)acetate	19518	2 g / 10 g
3-Trimethylsilyl-2-propyn-1-ol 99%	31389	1 g	Palladium (5%) on Carbon	19502	10 g / 100 g
4-(Trimethylsilyl)-3-butyn-2-one 98%	36780	5 g	Palladium (10%) on Carbon	19503	10 g / 50 g
(Triisopropylsilyl)acetylene 97%	36874	5 g / 25 g	Copper(I)iodide 99,995%	20150	5 g / 25 g / 100 g
Phenylacetylene 98%	15246	25 g / 100 g	Copper(I)iodide 98%	19490	250 g / 1 kg

Acros Organics offers currently more than 70 terminal alkynes.

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---

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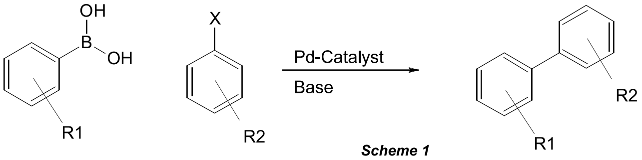
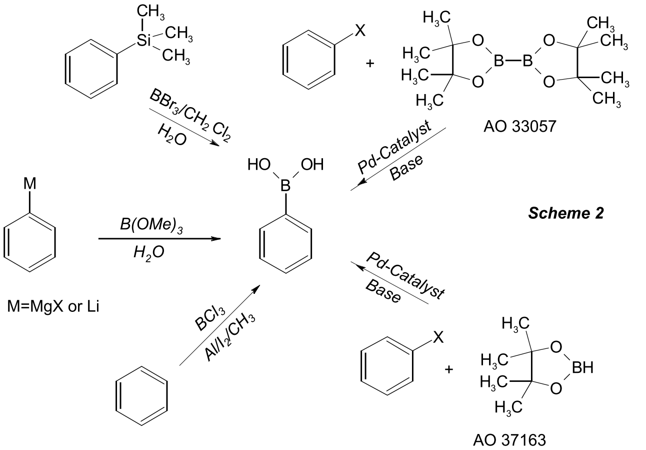
SUZUKI-REACTION[1]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (III)

Amongst the growing number of palladium-catalysed C-C-coupling reactions the Suzuki-Miyaura-reaction[2] plays a leading role. In this reaction an aryl-halogenide is coupled with a aryl- or vinyl-boronic acid or boronic-ester to unsymmetric biaryles (*Scheme 1*).



Scheme 1



Scheme 2

Major advantages of the Suzuki-reaction are

- The stability of the boron-reagents[3]
- The easy access to a broad variety boronic-acids through different synthetic pathways (*Scheme 2*)[4,5]
- The tolerance for different functional groups
- The simple experimental conditions.

The Suzuki-Miyaura-reaction was also extended to B-alkyl compounds[6]. The effects of the catalysts, ligands, solvents and substrates have been investigated[1,7]. The catalyst Tetrakis(triphenylphosphine)palladium is most common, but also other homogeneous catalysts as well as immobilised or heterogeneous[8] palladium-compounds have been used.

REAGENTS FROM ACROS ORGANICS USED FOR THE SUZUKI COUPLING

Bis(pinacolato)diboron	33057	Bis(triphenylphosphine)palladium(II) chloride	29925
Pinacolborane	37163	Bis(dibenzylideneacetone)palladium	29197
Catecholborane	18290	1,2-Bis(diphenylphosphino)ethane	14791
9-Borabicyclo[3.3.1]nonane	34634	1,3-Bis(diphenylphosphino)propane	31005
Palladium(II)acetate	19518	1,4-Bis(diphenylphosphino)butane	29646
Tetrakis(triphenylphosphine)palladium	20238	Triphenylphosphine, polymer supported	36684
Tris(dibenzylideneacetone)dipalladium(0)	37071	Triphenylphosphine, polymer supported	36687
Tetrakis(acetonitril)palladium(II) BF4-	36352	Bis(neopentylglycolato)diboron	35889
(1,1’Bis-(diphenylphosphino)-ferrocene) -		Bis(Hexylene glycolato)diboron	36634
palladiumdichloride “Pd(dppf)Cl2”	34868	Borontribromide 99,9%	29520
Palladium(II)chloride, 99.995%	36967	Borontribromide 99+%	36521
Borontribromide 1 M in Methylenchoride	19890	Borontrichloride 1 M in Hexane	19892
Borontrichloride 1 M in Methylenchloride	17668		

+ more than 160 Boronic acids and esters

---

[1] N.Miyaura, Advances in Metal-Organic Chemistry, JAI Press Inc. **1998**

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[3] Boronic acids and esters are crystalline, easy to handle, thermally stable, non-toxic and relatively inert to water and oxygen

[4] synthesis of arylboronic esters: T.Ishiyama, M.Murata, N. Miyaura J.Org.Chem. **1995** 60, 7508; T.Ishiyama, N. Miyaura, J.Organometal.Che,. 611 (**2000**) 392.

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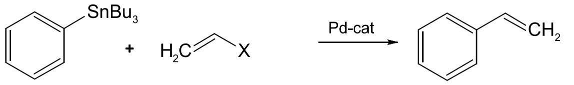
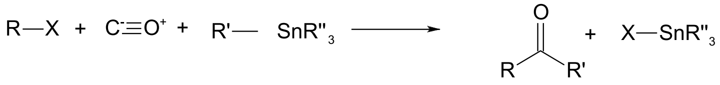
STILLE-REACTION [1,2]

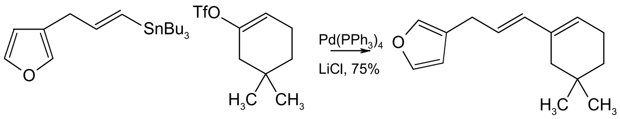
Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (IV)



The Stille-coupling is the palladium-catalyzed reaction between organo-stannanes and organic halides[3]. Typically the stannane is sp^2 or sp-hybridised (Aryl, alkenyl, alkinyl) but also alkyl-, allyl- and benzyl-stannanes and others have been used. The reactivity follows the order alkynyl > alkenyl > aryl > allyl ~ benzyl>alkyl. The halides are usually bromides or iodides (and also triflates), arylchlorides are less reactive but can be used in good yields with a catalyst-system $Pd_2(dba)_3$, CsF and tri-tert.Butylphosphine. The organic halides may be aryl, vinyl-, acyl-1[1,6,7] substituted[2]. In the presence of carbon monoxide the coupling happens with insertion of CO.



The Stille-coupling can be influenced by additives like copper[8]-, and silver[9]-salts and Lithium chloride[10]. The pathway of the reaction has been studied[11], the catalytic cycle is similar to other palladium-catalyzed cross-coupling reactions[2]. The Stille coupling has found many applications in organic synthesis, due to the broad scope and good tolerance against many functional groups. Some recent examples in totals synthesis: Synthesis of Amphidinolide A[12], Synthesis of Sanglifehrin A[13,14], Synthesis of Callipeltoside A[15], partly synthesis of Maitotoxine[16]. The Stille-reaction has been used with solid-supported reagents[17] as well as in ionic liquids[18].



Acros Organics offers a wide range of palladium-catalysts, phosphine-ligands and organo-tin-compounds for the Stille-coupling:

REAGENTS FROM ACROS ORGANICS USED FOR THE STILLE COUPLING

Copper(I)iodide, 99,995% anhydrous in Ampoules	**20150**
Copper(I)iodide, 98%	**19490**
Cesium fluoride 99,9%	**31591**
Cesium fluoride 99%	**18951**

Useful Palladium compounds for the Stille reaction:

Palladium(II) acetate 47,5% Pd	19518
Bis(triphenylphosphine)palladium(II)chloride 98%	29925
Tetrakis(triphenylphosphine)palladium(0), 99%	20238
Bis(triphenylphosphine)palladium(II) acetate, 99%	20927
Bis(dibenzylideneacetone)palladium	29197
Tris(dibenzylideneacetone)dipalladium(0), 97%	31877
Tris(dibenzylideneacetone)dipalladium-chloroform adduct	36934

Some Tin Compounds from Acros Organics:

Tetra-n-butyltin 96%	13798
Tri-n-butyltin chloride , tech. 90%	13935
Tri-n-butyltin hydride 97%	21573
Tri-n-butyltin cyanide 97%	21602
Triphenyltin hydride 95%	22378
Tributyl(vinyl)tin 96%	29423
Tributyl(vinyl)tin 97%	35000
Tributylethynylstannane 98%	29424
Hexa-n-butylditin 98%	35151
Tetraphenyltin 95%	36661
Hexamethylditin 99%	29585
Bis(tributylstannyl)acetylene	36958
Tributyl(3-methyl-2-butenyl)tin 90%	37022
Tributylphenyltin	37023

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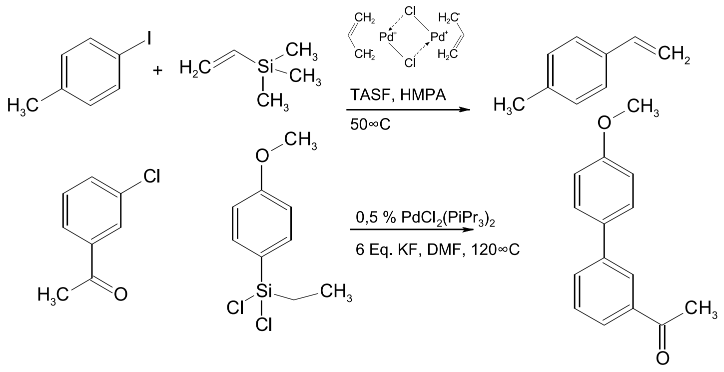
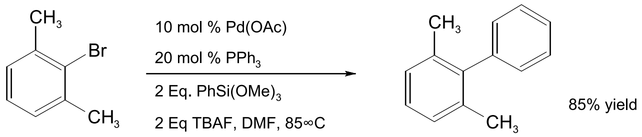
HIYAMA-COUPLING [1,2]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (V)



Recently the use of siloxanes and of silacyclobutanes[6] in the Hiyama-coupling has been reported. The reaction tolerates several functional groups and also different aromatic or vinylic systems can be transferred[7].

The Hiyama-Coupling is the palladium-catalysed reaction between aryl- and alkenyl- halogenides or -triflates with organo-silanes. The reaction rate is increased by activating the silane with fluoride and by using chloro- and fluorosilanes instead of trimethylsilanes[3]. Also microwaves have been used to accelerate the reaction rate[4]. The Hiyama-coupling is comparable with the Stille-coupling with the advantage of avoiding toxic tin-compounds in the reaction.



REAGENTS FOR THE HIYAMA COUPLING FROM **ACROS ORGANICS**

Vinyltrimethylsilane, 97%	20033
Tetravinylsilane, 97%	31373
Triethylvinylsilane, 97%	31377
1,1-Bis(trimethylsilyloxy)-2-trimethylsilylethene	33101
Triphenylvinylsilane, 95%	35099
(1-Bromovinyl)trimethylsilane, 97%	40328
Triethoxyvinylsilane, 97%	17461
Vinyltrimethoxysilane, 98%	21652
Vinyl tris(2-methoxyethoxy) silane, 96%	25051
Vinyltriacetoxysilane, monomer, 90%	25056
Vinyltris(trimethylsilyloxy)silane, 95%	33847

PALLADIUM CATALYSTS

Bis(triphenylphosphine)-palladium(II)chloride, 98%	29925
Allylpalladium chloride, dimer, 98%	20683
Tetrakis(triphenylphosphine)-palladium(0), 99%	20238

Phenyltrimethoxysilane	37064
Dichloromethylphenylsilane, 98%	14738
Tetrabutylammoniumfluoride, 1 M in tetrahydrofurane	20195
Tetrabutylammoniumfluoride, trihydrate, 99%	22108

A COMPREHENSIVE RANGE OF FLUORINATING AGENTS IS AVAILABLE AT ACROS ORGANICS.

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Dichloromethylvinylsilane, 97%	14743
Allyldichloromethylsilane, 97%	33819

AND MANY MORE SILANES, CHLOROSILANES AND SILOXANES...

---

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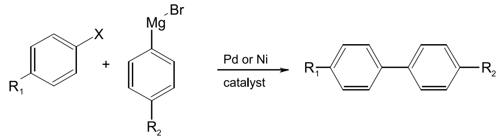
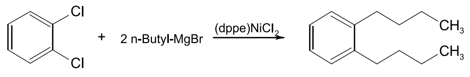
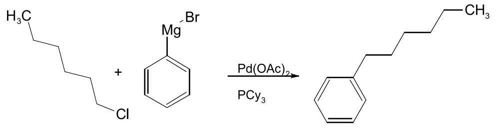
KUMADA-COUPLING [1,2,3]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (VI)





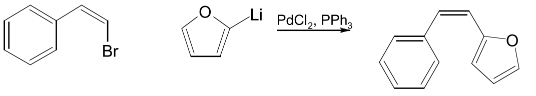


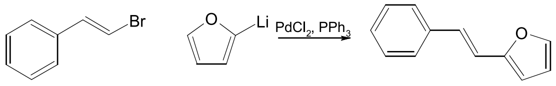
The Kumada-coupling is the nickel[4]- or palladium-catalysed reaction between aryl- and vinyl-halogenides or –triflates and aryl-, alkenyl- or alkyl- grignard-reagents[5,6]. Also heteroaryl-[7] and alkyl[8]-halides can be coupled with Grignard reagents.

The reactivity of the halogenides follows the order I > Br > Cl when Palladium is used as catalyst, whereas with certain nickel-catalysts the order is: Cl > I > Br[5].

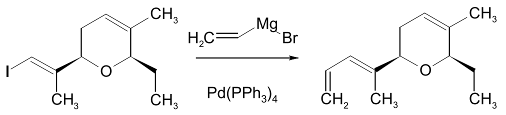
(Z)-Alkenyl-grignards couple non-stereospecific with nickel catalysts[2], but the reaction is stereospecific ("retention of configuration") with palladium-catalysts[9]. The phosphine-ligand has also a strong influence on the yield. Bidentate ligands generally bear a higher activity than monodentate phosphines. Bis(diphenylphosphino)propane (AO 31005) is optimal for most reactions[2].

The Kumada-coupling is somewhat limited because of the incompatibility of Grignard-reagents with certain functional groups[10].





Murahashi et al[11,12] have used numerous functionalized and non-functionalized organo-lithium compounds instead of Grignard-reagents for a Kumada-like coupling reaction.



In a recent example the Kumada coupling was used for an intermediate step in the total synthesis of (+)-Ambrucitin[13].

SOME CATALYSTS AND REAGENTS FROM ACROS ORGANICS FOR THE KUMADA COUPLING

Nickel & Palladium catalysts and Ligands

[1,3-Bis-Diphenylphosphino-propane] nickel(II)chloride, 99%	29159
Nickel acetylacetonate, 96%	12826
Bis(triphenylphosphine)nickel(II)chloride, 98%	21750
Tetrakis(triphenylphosphine)nickel(0), 95%	22398
[1,2-Bis-Diphenylphosphino-ethane] nickel (II) chloride	36323
Bis(triphenylphosphine)nickel(II)bromide, 99%	31632
Nickel(II) chloride hexahydrate, 99.9999%	19357
Nickel(II) chloride hexahydrate, p.a.	27051

1,2-Bis(dicyclohexylphosphino)ethane nickel(II) chloride	30116
1,1'-Bis-(diphenylphosphino)ferrocene	34801
1,2- Bis-(diphenylphosphino)ethane, 98+%	14791
1,3-Bis(diphenylphosphino)propane, 97%	31005
1,4-Bis-(diphenylphosphino)butane, 98%	29646
Bis(triphenylphosphine)palladium(II)chloride, 98%	29925
Tetrakis(triphenylphosphine)palladium(0), 99%	20238
1,1'-Bis(diphenylphosphino)ferrocene palladium(II)dichloride, complex with dichloromethane	34868

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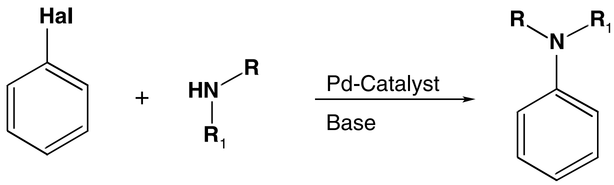
BUCHWALD-HARTWIG-REACTION [1]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (VII)



Hal: Halogenide or Triflate

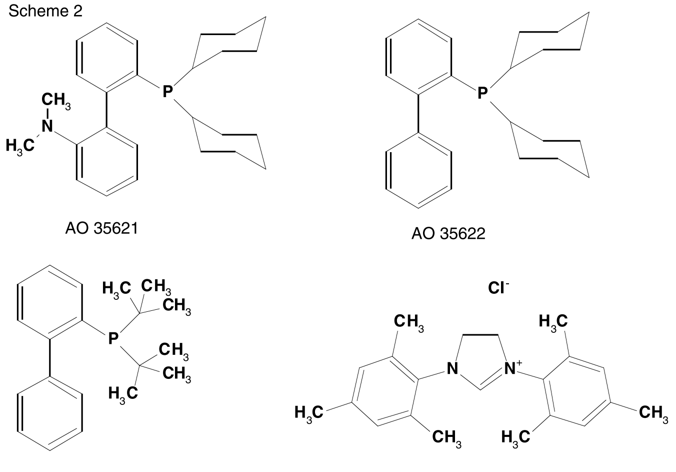
R_1: H, Alkyl, Aryl

Scheme 1

The transition metal catalyzed cross-coupling between aryl-halogenides[2,3], and -triflates[4] and primary or secondary amines to anilines is called the Buchwald-Hartwig[5] reaction (Scheme 1). By replacing the amines with alkoholes or phenoles the reaction leads to arylethers[6,7] although the rate determining "reductive elimination" step[8] is somewhat more difficult. The yields in the Buchwald-Hartwig reaction can be strongly improved by using sterically strongly hindered phosphine-ligands[1,9,10,11] or the very potent N-heterocyclic carbenes[12,13], which can be made from imidazolium salts as shown in Scheme 2.

With 1,1'-Bis(di-phenylphosphino)-ferrocene (AO 34801) as ligand and nickel on charcoal as heterogeneous catalyst the amination of arylchlorides was also succesful[14]. The Buchwald-Hartwig reaction in combination with the directed-ortho-metalation was used for the synthesis of acridones[15] and other heterocycles. The chemo- and regioselectivity of the Buchwald-Hartwig reaction was shown in the total synthesis of Isocryptolepine[16].

Scheme 2



AO 35621

AO 35622

AO 35623

AO 35619

SOME CATALYSTS AND REAGENTS FOR THE BUCHWALD-HARTWIG REACTION FROM ACROS ORGANICS

Tris(dibenzylideneacetone)dipalladium(0), 97%	31877
1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex	34868
Bis(benzonitrile)palladium(II) chloride, 99+%	20790
Palladium(II)acetate, 47.45% Pd	19518
Tetrakis(triphenylphosphine)palladium(0), 99%	20238
1,1'-Bis(diphenylphosphino)ferrocene	34801
Tri-o-tolyl-phosphine, 99%	42232
2-(Di-tert-butylphosphino)biphenyl, 99%	35621
2-(Dicyclohexylphosphino)biphenyl, 98%	35622
2- (Dicyclohexylphosphino)-2'-(N,N-dimethylamino)biphenyl, 97%	35623
1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride, 95%	35619

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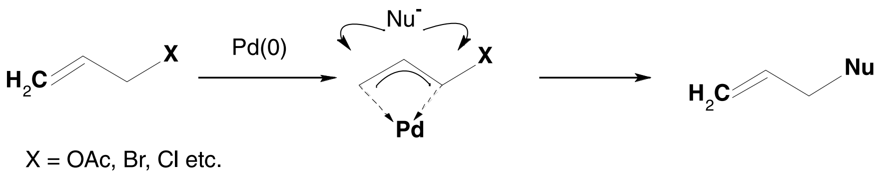
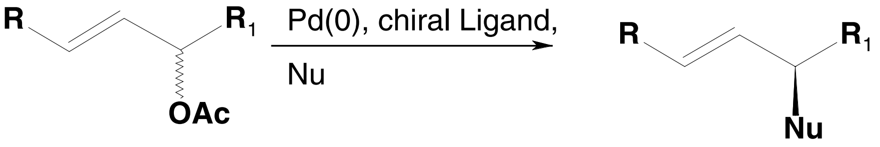
TSUJI-TROST-REACTION [1,2]

Precious-Metal catalysts from Acros Organics for coupling reactions in organic synthesis (VIII)



The Tsuji-Trost reaction is the widely used palladium catalysed substitution of allylic- or propargylic[3]-compounds with (carbon)-nucleophiles like enolates or other stabilised carbanions[4] such as α-sulfonyl-, α-nitro- or α-cyanocarbanions[4]. The reaction proceeds through allyl-palladium intermediates[5]. In the first example Tsuji[1] reported the reaction of allylpalladium chloride dimer (**AO 20683**) with ethylmalonate and ethylacetoacetate. A broad variety of allylic compounds can been used[4] although allyl-acetates are most common. The chemo-, regio- and stereoselectivity[6] of the Tsuji-Trost-reaction have been intensively studied[7]. The enantioselectivity with chiral phosphine-ligands[8,9,10,11,12,] was also featured by numerous extensive studies[13].

The allylic substitution can also be catalysed with other metal-complexes like [Ir(COD)Cl][14] (**AO 36938**) and especially some tungsten and molybdenum complexes, which can react with opposite regioselectivity compared with the palladium complexes[15,16].



REAGENTS FROM ACROS ORGANICS FOR THE TSUJI-TROST REACTION

Allylpalladium chloride dimer, 98%	20683
Tetrakis(triphenylphosphine)palladium(0), 99%	20238
Tris(dibenzylideneacetone)dipalladium-chloroform adduct	36934
Bis(triphenylphosphine)palladium(II)chloride, 98%	29925
Palladium(II) acetate, 47.5% Pd	19518
Chlorobis(cyclooctene)iridium(I), dimer, 97%	36938
Allyl acetate, 99%	18065
Neryl acetate, 97%	37640
trans-2-Hexenyl acetate, 98%	31053
3,4-Diacetoxy-1-butene, 97%	40631

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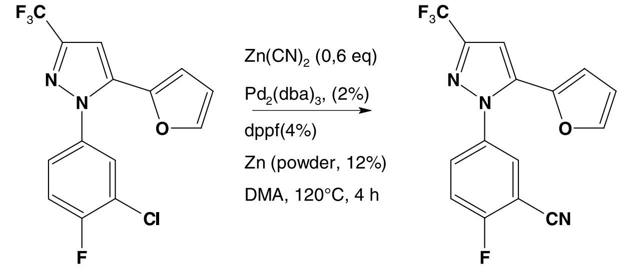
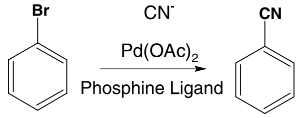
CYANATION OF AROMATIC HALIDES

Precious-metal catalysts from Acros Organics for coupling reactions in organic synthesis (IX)

Aromatic nitriles are important pharmaceuticals[1] and agrochemicals and are also key-intermediates for the synthesis of carboxylic acids, benzyl amines and other important chemicals. The substitution of aromatic halides by cyanide is, amongst others[2], a general route to make aromatic nitriles.



Lit. 14a



The well known synthesis via the Rosenmund-von-Braun-reaction[3,4] with stoichiometric amounts of copper(I)cyanide requires unfortunately harsh reaction conditions. The catalytical reactions with nickel[5,6,7]- and palladium[8,9,10,11,12] compounds have recently opened a direct and rapid approach to aromatic nitriles. These reactions proceed at relatively mild conditions and have, depending on the reaction conditions, partly very good yields.

A limitation is the fact that the catalyst is often deactivated by cyanide-ions[6,13]. Another limit is the low reactivity of the cheap and easily available aryl-chlorides with palladium-catalysts[1,14]. Both problems which can be overcome by the right choice of the reaction conditions, solvents and reagents[6,13].

SOME REAGENTS FROM ACROS ORGANICS FOR THE CATALYTIC CYANATION

Cyanides

Zinc cyanide, 98%	36807
Trimethylsilyl cyanide, 98%	19956
Potassium cyanide, p.a.	19660
Sodium cyanide, ACS	42430
Copper(I) cyanide, 99%	20208

Phosphine ligands/Additives

1,5-Bis(diphenylphosphino)pentane, 97%	32085
1,4-Bis(diphenylphosphino)butane, 98%	29646
1,1'-Bis(diphenylphosphino)ferrocene	34801
Copper(I) iodide, 99.995%	20150
N,N,N',N'-Tetramethylethylenediamine, 99%	13845
Cobalt(II) chloride, anhydrous, 97%	21413

Nickel and palladium catalysts

Palladium(II) acetate, 47.5% Pd	19518
Palladium(II) chloride, 59% Pd	19520
Bis(dibenzylideneacetone)palladium	29197
Bis(triphenylphosphine)nickel(II)chloride 98%	21750
Bis(triphenylphosphine)nickel(II)bromide 99%	31632
Tetrakis(triphenylphosphine)palladium(0), 99%	20238
[1,3-Bis(diphenylphosphino)propane]nickel(II)chloride, 97%	29159
Nickel(II) bromide, 99%	20336

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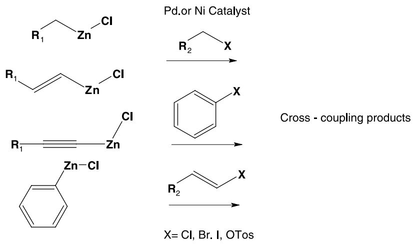
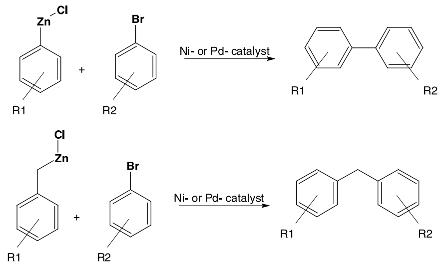
NEGISHI-COUPLING[1,2]

Precious-metal catalysts from Acros Organics for coupling reactions in organic synthesis (X)

The Negishi-coupling is a widely used nickel[3]- or palladium-catalysed reaction for the synthesis of unsymmetrical biaryls[4] and biaryl-methanes[5] from arylzinc halides or benzylic zinc halides.

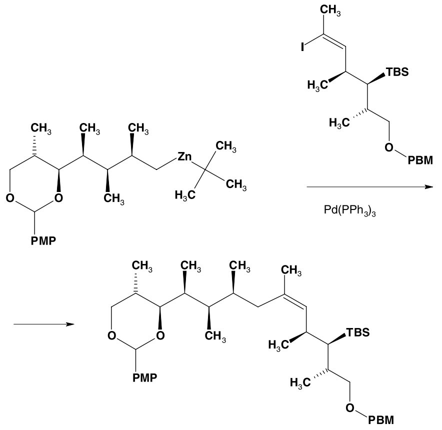
Alkyl-[6,7,8,9,10] alkenyl-[11,12] and alkynyl-[13] zinc halides can also be used for the coupling as well as wide variety of substrates like aryl-, alkyl- and alkenyl[14] halides and -tosylates[7]. Also heterocycles like halogen furans and halogenated thiazoles have been utilized successfully[15].





Besides the broad scope of reactants also many functional groups can be present in the molecules[16,17,18] because the zinc-organic compounds are much more tolerant than lithium- or magnesium-organic compounds. The zinc-reagents[19] for use in the Negishi-coupling can be prepared by direct insertion[20] or exchange-reactions[16].

Due to the mildness, (stereo- and chemo-) selectivity and high yields the Negishi-coupling has been successfully used in the synthesis of complex molecules[21]. A recent example is the formation of a key intermediate in the total synthesis of (+)-discoderminolide[22].



USEFUL PRODUCTS FOR THE NEGISHI-COUPLING FROM ACROS ORGANICS

Tetrakis(triphenylphoshine)palladium(0), 99%	20238	Dimethylzinc, 2.0M solution in toluene	37724
Bis(triphenylphosphine)palladium(II)chloride, 15% Pd	19732	Diethylzinc, 15 wt.% solution in hexane	20551
Bis(triphenylphosphine)palladium(II)chloride, 98%	29925	Diethylzinc, 1.5M solution in toluene	37731
Nickelacetylacetonate, 96%	12826	Tri-o-tolylphosphine, 99%	42232
Zinc, 5% suspension in THF, highly active Rieke® metal	36917	Tri-m-tolylphosphine, 98%	31728
Zinc chloride, 1.0M solution in diethyl ether	37005	Tri-p-tolylphosphine, 95%	42233
Zinc chloride, 0.5M solution in THF	37006	Tricyclohexyl phosphine, 97%	42161

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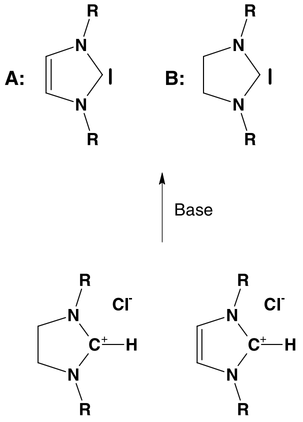
N-HETEROCYCLIC CARBENES

AS NEW LIGANDS FOR CROSS-COUPLING AND METATHESIS REACTIONS

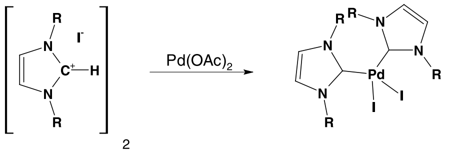
Precious-metal catalysts from Acros Organics for coupling reactions in organic synthesis (XI)

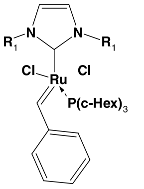
N-heterocyclic carbenes (NHC) have emerged as a new class of σ-donor ligands with similar and even superior electronic characteristics as phosphine-ligands[1]. The NHC's A and B can be easily prepared from the corresponding imidazolium-ions and imidazolidinium ions with base[2,3,4,5].



In the presence of a suitable metal the NHC form complexes[6] which are very useful as catalysts for cross-coupling reactions[7] (i.e. with palladium) or methatesis-[8,9,10] reactions (with Ruthenium).

Compared with phosphine ligands, the NHC-metal complexes have a very high catalytical activity combined with a improved stability and endurance of the catalyst under reaction conditions[7].

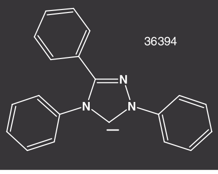




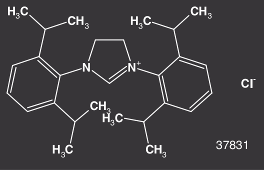
Grubb's second generation catalyst

SOME EXAMPLES FOR N-HETEROCYCLIC CARBENES AND CARBENE-PRECURSORS FROM ACROS ORGANICS

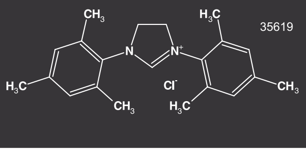
1,3,4-Triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene	36394
1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride, 95%	35619
1,3-Bis(2,6-diisopropylphenyl)-imidazolium chloride	37831
1,3-Diadamantyl-imidazolium chloride	37832
1,3-Bis(2,4,6-trimethylphenyl)-imidazolidinium chloride	37833
1,3-Bis(2,6-diisopropylphenyl)-imidazolidinium chloride	37834



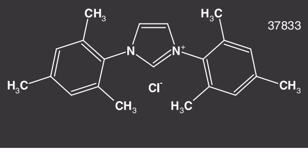
36394



37831



35619



37833

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