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COUPLING REACTIONS WITH CATALYSTS AND REAGENTS FROM ACROSS 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.

Some prominent examples for modern catalytical reactions are:

- Hydrosilylations
- Carbonylations and decarbonylations
- Asymmetric hydrogenations
- Selective oxidations
- Alkene-methathesis
- 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

\[ \text{Ar} \overset{X}{\underset{\text{Pd (0)}}{\text{+}}} \]

\[ X = \text{Hal, Tosylate} \]
Most of these coupling reactions have a similar catalytic cycle:

Step 1: Oxidative Addition

The oxidative addition is the rate determining step. The reactivity of the halogenides follows the order:

$I >> (OSO_2CF_3) > Br >> Cl$

in most coupling reactions.

Step 2: Transmetallation with base

$M = H$ or Metal

Step 3: Cis-trans-isomerisation

Step 4: Reductive Elimination

The Heck-reaction differs slightly:

Step 1: Oxidation addition

Step 2: Olefin Insertion

Step 3: β-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.
HECK-REACTION

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. In the Heck-reaction an alkene (1) is coupled with a aryl- or alkenyl-halogenide (2) to vinylarenes or dienes (3) (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 of palladium-salts in the presence of a suitable phosphine-ligand.

Because of the oxidative addition of R-X to the Pd(PPh3)2⁺ (Scheme 2) the rate determining step is the reactivity of the halogenides (Arl > ArBr > ArCl).

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.

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

Chiral ligands like (R)- or (S)- Binap have been used for an enantioselective Heck-reaction (Scheme 3).

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

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Purity</th>
<th>Quantity 1</th>
<th>Quantity 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrakis(triphenylphosphine)palladium(0) 99%</td>
<td>20238</td>
<td>1 g / 5 g</td>
<td>20238</td>
</tr>
<tr>
<td>Palladium(II) acetate 47.5% Pd</td>
<td>19518</td>
<td>2 g / 10 g</td>
<td>19518</td>
</tr>
<tr>
<td>Palladium(II) chloride 59% Pd</td>
<td>19520</td>
<td>5 g</td>
<td>19520</td>
</tr>
<tr>
<td>Palladium(II) chloride 99.999%</td>
<td>36967</td>
<td>1 g / 5 g</td>
<td>36967</td>
</tr>
<tr>
<td>Bis(triphenylphosphine)palladium(II) chloride 15% Pd</td>
<td>19732</td>
<td>1 g / 5 g</td>
<td>19732</td>
</tr>
<tr>
<td>Bis(triphenylphosphine)palladium(II) chloride 98%</td>
<td>29925</td>
<td>250 mg / 5 g</td>
<td>29925</td>
</tr>
<tr>
<td>Tris(dibenzyldieneacetone)dipalladium(II) 97%</td>
<td>31877</td>
<td>500 mg / 5 g</td>
<td>31877</td>
</tr>
<tr>
<td>Tris(dibenzyldieneacetone)palladium</td>
<td>29197</td>
<td>1 g / 5 g</td>
<td>29197</td>
</tr>
<tr>
<td>Bis(triphenylphosphine)palladium(II) acetate 99%</td>
<td>20927</td>
<td>1 g / 5 g</td>
<td>20927</td>
</tr>
<tr>
<td>(R)(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 99%</td>
<td>26553</td>
<td>250 mg</td>
<td>26553</td>
</tr>
<tr>
<td>(S)(-)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 99%</td>
<td>26554</td>
<td>250 mg</td>
<td>26554</td>
</tr>
<tr>
<td>(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl</td>
<td>36864</td>
<td>5 g</td>
<td>36864</td>
</tr>
<tr>
<td>Bis(tri-t-butylphosphine)palladium(0) 98%</td>
<td>20927</td>
<td>1 g / 5 g</td>
<td>20927</td>
</tr>
<tr>
<td>Bis(tricyclohexylphosphine)palladium(0)</td>
<td>42233</td>
<td>5 g</td>
<td>42233</td>
</tr>
<tr>
<td>Tri-o-tolylphosphine 99%</td>
<td>42232</td>
<td>5 g</td>
<td>42232</td>
</tr>
<tr>
<td>Tris(4-methoxyphenyl)phosphine 95%</td>
<td>42224</td>
<td>10 g</td>
<td>42224</td>
</tr>
<tr>
<td>Tris(4-chlorophenyl)phosphine 97%</td>
<td>42221</td>
<td>2 g</td>
<td>42221</td>
</tr>
<tr>
<td>Trisopropylphosphine 98%</td>
<td>31733</td>
<td>1 g / 5 g</td>
<td>31733</td>
</tr>
<tr>
<td>Tri-tert-butylphosphine 95%</td>
<td>36967</td>
<td>1 g / 5 g</td>
<td>36967</td>
</tr>
<tr>
<td>Trimesitylphosphine 97%</td>
<td>32113</td>
<td>1 g</td>
<td>32113</td>
</tr>
<tr>
<td>Tris(2,6-dimethoxyphenyl)phosphine</td>
<td>36496</td>
<td>5 g / 25 g</td>
<td>36496</td>
</tr>
<tr>
<td>Tricyclohexyl phosphine 97%</td>
<td>42161</td>
<td>5 g</td>
<td>42161</td>
</tr>
</tbody>
</table>

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

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SONOGASHIRA-REACTION

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

The Sonogashira-reaction and the closely related Stephens-Castro reaction consists of the palladium-catalysed coupling of copper-acetylides and arylhalogenides to yield alkynylarenes (Scheme 1).

This reaction is one of the most important reactions to produce alkenyl- and aryl-acetylenes, which have recently got a lot of attention as endyln-antibiotics (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-arylethylenes (Scheme 3).

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

Catalysts and Reagents from Acros Organics for the Sonogashira-REACTION

<table>
<thead>
<tr>
<th>(Triethylsilyl)acetylene</th>
<th>36873</th>
<th>1 g / 5 g</th>
<th>Bis(benzonitrile)palladium(II) chloride</th>
<th>20790</th>
<th>1 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethylacetylene 98%</td>
<td>20357</td>
<td>5 g / 25 g</td>
<td>Bis(triphenylphosphine)palladium(II) chloride 98%</td>
<td>29825</td>
<td>2 g / 5 g</td>
</tr>
<tr>
<td>1-(Trimethylsilyl)-1-propyne 98%</td>
<td>22353</td>
<td>1 g / 5 g</td>
<td>Tetrakis(triphenylphosphine)palladium(0) 99%</td>
<td>20238</td>
<td>1 g / 5 g</td>
</tr>
<tr>
<td>1,4-Bis(trimethylsilyl)-1,3-butadiyne 98%</td>
<td>22539</td>
<td>5 g</td>
<td>Palladium(II)acetate</td>
<td>19518</td>
<td>2 g / 10 g</td>
</tr>
<tr>
<td>3-Trimethylsilyl-2-propyn-1-ol 99%</td>
<td>31389</td>
<td>1 g</td>
<td>Palladium (5%) on Carbon</td>
<td>19502</td>
<td>10 g / 100 g</td>
</tr>
<tr>
<td>4-(Trimethylsilyl)-3-butyne-2-one 98%</td>
<td>36870</td>
<td>5 g</td>
<td>Palladium (10%) on Carbon</td>
<td>19503</td>
<td>10 g / 50 g</td>
</tr>
<tr>
<td>(Trisopropylsilyl)acetylene 97%</td>
<td>36874</td>
<td>5 g / 25 g</td>
<td>Copper(I)iodide 99.995%</td>
<td>20150</td>
<td>5 g / 25 g / 100 g</td>
</tr>
<tr>
<td>Phenylacetylene 98%</td>
<td>15246</td>
<td>25 g / 100 g</td>
<td>Copper(I)iodide 98%</td>
<td>19490</td>
<td>250 g / 1 kg</td>
</tr>
</tbody>
</table>

Acros Organics offers currently more than 70 terminal alkynes.

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SUZUKI-REACTION

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 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).

Major advantages of the Suzuki-reaction are

• The stability of the boron-reagents
• The easy access to a broad variety of boronic-acids through different synthetic pathways (Scheme 2)
• The tolerance for different functional groups
• The simple experimental conditions.

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

REAGENTS FROM ACROS ORGANICS USED FOR THE SUZUKI COUPLING

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Code</th>
<th>CAS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis(pinacolato)diboron</td>
<td>33057</td>
<td>29925</td>
</tr>
<tr>
<td>Pinacolborane</td>
<td>37163</td>
<td>29197</td>
</tr>
<tr>
<td>Catecholborane</td>
<td>18290</td>
<td>1,2-Bis(diphenylphosphino)ethane</td>
</tr>
<tr>
<td>9-Borabicyclo[3.3.1]nonane</td>
<td>34634</td>
<td>1,3-Bis(diphenylphosphino)propane</td>
</tr>
<tr>
<td>Palladium(II)acetate</td>
<td>19518</td>
<td>1,4-Bis(diphenylphosphino)butane</td>
</tr>
<tr>
<td>Tetrakis(triphenylphosphine)palladium</td>
<td>20238</td>
<td>Triphenylphosphine, polymer supported</td>
</tr>
<tr>
<td>Tris(dibenzylideneacetone)dipalladium(0)</td>
<td>37071</td>
<td>Triphenylphosphine, polymer supported</td>
</tr>
<tr>
<td>Tetrakis(acetonitril)palladium(II) BF4-</td>
<td>36352</td>
<td>Bis(neopentylglycolato)diboron</td>
</tr>
<tr>
<td>(1,1’Bis-(diphenylphosphino)-ferrocene) - palladium dichloride “Pd(dppf)Cl2”</td>
<td>34868</td>
<td>Bis(hexylene glycolato)diboron</td>
</tr>
<tr>
<td>Palladium(II)chloride, 99.995%</td>
<td>36967</td>
<td>Borontribromide 99.9%</td>
</tr>
<tr>
<td>Borontribromide</td>
<td>36521</td>
<td>Borontribromide 99+%</td>
</tr>
<tr>
<td>Borontrichloride 1 M in Methylenchloride</td>
<td>19890</td>
<td>Borontrichloride 1 M in Hexane</td>
</tr>
<tr>
<td>Borontrichloride 1 M in Methylenchloride</td>
<td>17668</td>
<td></td>
</tr>
</tbody>
</table>

+ more than 160 Boronic acids and esters

---

2 Boronic acids and esters are crystalline, easy to handle, thermally stable, non-toxic and relatively inert to water and oxygen
5 For a synthesis without phosphine-ligands; Org Synthesis Vol 75, 61
7 Major advantages of the Suzuki-reaction are
• The stability of the boron-reagents
• The easy access to a broad variety of boronic-acids through different synthetic pathways (Scheme 2)
• The tolerance for different functional groups
• The simple experimental conditions.
The stille-coupling is the palladium-catalyzed reaction between organo-stannanes and organic halides. Typically the stannane is sp² or sp-hybridised (aryl, alkenyl, alkynyl) 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 Pd₂(dba)₃, CsF and tri-tert. Butylphosphine. The organic halides may be aryl, vinyl-, acyl- substituted. In the presence of carbon monoxide the coupling happens with insertion of CO.

The stille-coupling can be influenced by additives like copper and silver-salts and lithium chloride. The pathway of the reaction has been studied, the catalytic cycle is similar to other palladium-catalyzed cross-coupling reactions. 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, Synthesis of Sanglifehrin A, Synthesis of Callipeltoside A, partly synthesis of Maitotoxine. The Stille-reaction has been used with solid-supported reagents as well as in ionic liquids.

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

![Chemical structures](image)

**REAGENTS FROM ACROS ORGANICS USED FOR THE STILLE COUPLING**

**Useful Palladium compounds for the Stille reaction:**
- Palladium(0) acetate 47,5% Pd 19518
- Bistriphenylphosphine) palladium(0) chloride 98% 29925
- Tetrakis(triphenylphosphine) palladium(0), 99% 20238
- Bistriphenylphosphine) palladium(0) acetate, 99% 20927
- Bis(dibenzylideneacetone)palladium 29197
- Tris(dibenzylideneacetone)dipalladium 97% 31877
- Tris(dibenzylideneacetone)dipalladium-chloroform adduct 36934

**Some Tin Compounds from Acros Organics:**
- Tetra-n-butylin 96% 13798
- Tri-n-butylin chloride, tech. 90% 13935
- Tri-n-butylin hydride 97% 21573
- Tri-n-butylin cyanide 97% 21602
- Triphenyltin hydride 95% 22378
- Tributyl(vinyl)tin 96% 29423
- Tri(tributylstannyl)acetylene 19518
- Hexamethylditin 99% 29585
- Bis(tributylstannyl)acetylene 29658
- Tributyl(3-methyl-2-butenyl)tin 90% 37022
- Tributylphosphine 37023

---

3. Acetate and triflate are possible.
HIYAMA-COUPLING ¹,²

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

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. Also microwaves have been used to accelerate the reaction rate. The Hiyama-coupling is comparable with the Stille-coupling with the advantage of avoiding toxic tin-compounds in the reaction.

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

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinyltrimethylsilane, 97%</td>
<td>20033</td>
</tr>
<tr>
<td>Tetravinylsilane, 97%</td>
<td>31373</td>
</tr>
<tr>
<td>Triethylvinylsilane, 97%</td>
<td>31377</td>
</tr>
<tr>
<td>1,1-Bis(trimethylsilyloxy)-2-trimethylsilyl-ethene</td>
<td>33101</td>
</tr>
<tr>
<td>Triphenylinylsilane, 95%</td>
<td>35099</td>
</tr>
<tr>
<td>(1-Bromovinyl)trimethylsilane, 97%</td>
<td>40328</td>
</tr>
<tr>
<td>Triethoxyvinylsilane, 97%</td>
<td>17461</td>
</tr>
<tr>
<td>Vinyltrimethylsilane, 98%</td>
<td>21652</td>
</tr>
<tr>
<td>Vinyl tris(2-methoxyethoxy) silane, 96%</td>
<td>25051</td>
</tr>
<tr>
<td>Vinyltriacetoxy silane, monomer, 90%</td>
<td>25056</td>
</tr>
<tr>
<td>Vinyltris(trimethylsilyloxy) silane, 95%</td>
<td>33847</td>
</tr>
<tr>
<td>Phenyltrimethoxysilane</td>
<td>37064</td>
</tr>
<tr>
<td>Dichloromethylphenylsilane, 98%</td>
<td>14738</td>
</tr>
<tr>
<td>Tetraethylaminiumfluoride, 1 M in tetrahydrofuran</td>
<td>20195</td>
</tr>
<tr>
<td>Tetraethylaminiumfluoride, trihydrate, 99%</td>
<td>22108</td>
</tr>
</tbody>
</table>

**PALLADIVM CATALYSTS**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis(triphenylphosphine)-palladium(II)chloride, 98%</td>
<td>29925</td>
</tr>
<tr>
<td>Allylpalladium chloride, dimer, 98%</td>
<td>20683</td>
</tr>
<tr>
<td>Tetrakis(triphenylphosphine)-palladium(0), 99%</td>
<td>20238</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Compound</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytrichlorosilane, 95%</td>
<td>13100</td>
</tr>
<tr>
<td>Dichloromethylvinylsilane, 97%</td>
<td>14743</td>
</tr>
<tr>
<td>Allyldichloromethylsilane, 97%</td>
<td>33819</td>
</tr>
</tbody>
</table>

AND MANY MORE SILANES, CHLOROSILANES AND SILOXANES...

⁵ P. Choong, C. J. Hardy, M. E. Mowery, Pure Appl. Chem. 9, 2000, 1655.
The Kumada-coupling is the nickel4- or palladium-catalysed reaction between aryl- and vinyl-halogenides or –triflates and aryl-, alkenyl- or alkyl- grignard-reagents 5,6. Also heteroaryl7 and alkyl8-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 > Br5.

(Z)-Alkenyl-grignards couple non-stereospecific with nickel catalysts 2, but the reaction is stereospecific (“retention of configuration”) with palladium-catalysts9. 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 9.

The Kumada-coupling is somewhat limited because of the incompatibility of Grignard-reagents with certain functional groups10.

Murahashi et al11,12 have used numerous functionalized and non-functionalized organolithium 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 (+)-Ambrucitin13.

The transition metal catalyzed cross-coupling between aryl-halogenides and triflates and primary or secondary amines to anilines is called the Buchwald-Hartwig reaction (Scheme 1). By replacing the amines with alcohols or phenols the reaction leads to arylethers, although the rate determining “reductive elimination” step is somewhat more difficult. The yields in the Buchwald-Hartwig reaction can be strongly improved by using sterically strongly hindered phosphine-ligands or the very potent N-heterocyclic carbenes, 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 successful. The Buchwald-Hartwig reaction in combination with the directed-ortho-metalation was used for the synthesis of acridones and other heterocycles. The chemo- and regioselectivity of the Buchwald-Hartwig reaction was shown in the total synthesis of Isocryptolepine.

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TSUJI-TROST-REACTION

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 compounds with (carbon)-nucleophiles like enolates or other stabilised carbanions such as α-sulfonyl-, α-nitro- or α-cyanocarbanions. The reaction proceeds through allyl-palladium intermediates. In the first example Tsuji reported the reaction of allylpalladium chloride dimer (AO 20683) with ethylmalonate and ethylacetacacetate. A broad variety of allylic compounds can be used although allyl-acetates are most common. The chemo-, regio- and stereoselectivity of the Tsuji-Trost-reaction have been intensively studied. The enantioselectivity with chiral phosphine-ligands was also featured by numerous extensive studies.

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

Reagents from Acros Organics for the Tsuji-Trost Reaction

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allylpalladium chloride dimer, 98%</td>
<td>20683</td>
</tr>
<tr>
<td>Tetrakis(triphenylphosphine)palladium(0), 99%</td>
<td>20238</td>
</tr>
<tr>
<td>Tris(dibenzylideneacetone)dipalladium-chloroform adduct</td>
<td>36934</td>
</tr>
<tr>
<td>Bis(triphenylphosphine)palladium(II)chloride, 98%</td>
<td>29925</td>
</tr>
<tr>
<td>Palladium(II) acetate, 47.5% Pd</td>
<td>19518</td>
</tr>
<tr>
<td>Chlorobis(cyclooctene)iridium(II), dimer, 97%</td>
<td>36938</td>
</tr>
<tr>
<td>Allyl acetate, 99%</td>
<td>18065</td>
</tr>
<tr>
<td>Neryl acetate, 97%</td>
<td>37640</td>
</tr>
<tr>
<td>trans-2-Hexenyl acetate, 98%</td>
<td>31053</td>
</tr>
<tr>
<td>3,4-Diacetoxy-1-butene, 97%</td>
<td>40631</td>
</tr>
</tbody>
</table>

References:

CYANATION OF AROMATIC HALIDES

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

Aromatic nitriles are important pharmaceuticals 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, a general route to make aromatic nitriles.

The well known synthesis via the Rosenmund-von-Braun-reaction with stoichiometric amounts of copper(i)cyanide requires unfortunately harsh reaction conditions. The catalytical reactions with nickel and palladium 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. Another limit is the low reactivity of the cheap and easily available aryl-chlorides with palladium-catalysts. Both problems which can be overcome by the right choice of the reaction conditions, solvents and reagents.

SOME REAGENTS FROM ACROS ORGANICS FOR THE CATALYTIC CYANATION

<table>
<thead>
<tr>
<th>Cyanides</th>
<th>Phosphine ligands/Additives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc cyanide, 98%</td>
<td>1,5-Bis(diphenylphosphino)pentane, 97%</td>
</tr>
<tr>
<td>Trimethylsilyl cyanide, 98%</td>
<td>1,4-Bis(diphenylphosphino)butane, 98%</td>
</tr>
<tr>
<td>Potassium cyanide, p.a.</td>
<td>1,1'-Bis(diphenylphosphino)ferrocene</td>
</tr>
<tr>
<td>Sodium cyanide, ACS</td>
<td>Copper(i) iodide, 99.995%</td>
</tr>
<tr>
<td>Copper(I) cyanide, 99%</td>
<td>N,N,N',N'-Tetramethylethylenediamine, 99%</td>
</tr>
</tbody>
</table>

Nickel and palladium catalysts

| Palladium(II) acetate, 47.5% Pd | Tetrakis(triphenylphosphine)palladium(0), 99% |
| Palladium(II) chloride, 59% Pd | [1,3-Bis(diphenylphosphino)propane]nickel(II)chloride, 97% |
| Bis(dibenzylideneacetone)palladium | Nickel(II) bromide, 99% |
| Bis(triphenylphosphine)nickel(II)chloride 98% | 20238 |
| Bis(triphenylphosphine)nickel(II)bromide 99% | 20336 |
**NEGISHI-COUPLING**

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

The Negishi-coupling is a widely used nickel3- or palladium-catalysed reaction for the synthesis of unsymmetrical biaryl4 and biaryl-methanes5 from arylzinc halides or benzylic zinc halides.

Alkyl-6.7.9,10 and alkenyl-11,12,13 zinc halides can also be used for the coupling as well as wide variety of substrates like aryl-, alkyl- and alkenyl14 halides and -tosylates7. Also heterocycles like halogen furans and halogenated thiazoles have been utilized successfully15.

Due to the mildness, (stereo- and chemo-) selectivity and high yield the Negishi-coupling has been successfully used in the synthesis of complex molecules16. A recent example is the formation of a key intermediate in the total synthesis of (+)-discoderminolide22.

Besides the broad scope of reactants also many functional groups can be present in the molecules6.16.17.18 because the zinc-organic compounds are much more tolerant than lithium- or magnesium-organic compounds. The zinc-reagents19 for use in the Negishi-coupling can be prepared by direct insertion20 or exchange-reactions16.

**USEFUL PRODUCTS FOR THE NEGISHI-COUPLING FROM ACROS ORGANICS**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Catalog Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethylzinc, 2.0M solution in toluene</td>
<td>37724</td>
</tr>
<tr>
<td>Diethylzinc, 15 wt.% solution in hexane</td>
<td>20551</td>
</tr>
<tr>
<td>Diethylzinc, 1.5M solution in toluene</td>
<td>37731</td>
</tr>
<tr>
<td>Tri-o-tolylphosphine, 99%</td>
<td>42232</td>
</tr>
<tr>
<td>Tri-m-tolylphosphine, 98%</td>
<td>31728</td>
</tr>
<tr>
<td>Tri-p-tolylphosphine, 95%</td>
<td>42233</td>
</tr>
<tr>
<td>Tricyclohexyl phosphine, 97%</td>
<td>42161</td>
</tr>
</tbody>
</table>

N-HETERO CYCLIC CARBENES
AS NEW LIGANDS FOR CROSS-CO UPL I NG AND METATHESIS RE ACTIONS
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. The NHC’s A and B can be easily prepared from the corresponding imidazolium-ions and imidazolidinium ions with base.

In the presence of a suitable metal the NHC form complexes which are very useful as catalysts for cross-coupling reactions (i.e. with palladium) or metathesis reactions (with Ruthenium).

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

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

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

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4 W.A.Herrmann, Ch. Kücher, Angew.Chem. 1997, 109, 2256
9 A.Franklin, Angew.Chem. 2000, 112, 3140