



**Science of  
Synthesis**

# Knowledge Updates 2016/2

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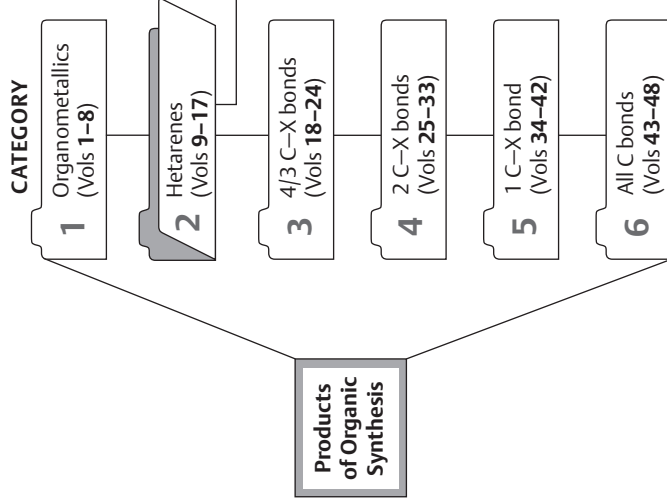
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## Organizational Structure of Science of Synthesis\*



Classification is **based on the product**, with all products belonging to one of six broad-ranging categories. All products occupy a strict hierarchical position in Science of Synthesis, defined according to the classification principles\*. Products in Categories 3–6 are organized according to oxidation state, with products containing the greatest number of carbon–heteroatom (C–X) or C–C  $\pi$ -bonds to a single carbon occupying the highest positions (e.g., carboxylates, enolates, and alcoholates are covered in Categories 3, 4, and 5, respectively).

Each category is subdivided into volumes (see opposing page), each of which is devoted to discrete groupings of compounds called **product classes** (e.g., “Thiophenes” is Product Class 10 of Volume 9). Product classes may be further subdivided into **product subclasses**, (e.g., “Thiophene 1,1-Dioxides” is Product Subclass 3 of Product Class 10 of Volume 9). Consequently, the relationship between heading name and heading number varies below product class level within individual volumes.

For each product class or subclass, a number of methods are described for synthesizing the general product type. Often there are variations on a method given. Both methods and variations contain experimental procedures with relevant background information and literature references. **Selected products and reactions** display the scope and limitations of the methods.

\* A complete description of the full classification principles can be found in the **Science of Synthesis Guidebook**.

**CATEGORY**
**UPDATED VOLUMES**

<b>1</b> Organometallics (Vols <b>1-8</b> )	1	2	3	4	5	6	7	8a	8b
<b>2</b> Heterarenes (Vols <b>9-17</b> )	9	10	11	12	13	14	15	16	17
<b>3</b> 4/3 C-X bonds (Vols <b>18-24</b> )	18	19	20a	20b	21	22	23	24	
<b>4</b> 2 C-X bonds (Vols <b>25-33</b> )	25	26	27	28	29	30	31a	31b	32
<b>5</b> 1 C-X bond (Vols <b>34-42</b> )	34	35	36	37	38	39	40a	40b	41
<b>6</b> All C bonds (Vols <b>43-48</b> )	43	44	45a	45b	46	47a	47b	48	

- 1 Compounds with Transition Metal-Carbon  $\pi$ -Bonds and Compounds of Groups 10-8 (Ni, Pd, Pt, Co, Rh, Ir, Fe, Ru, Os)
- 2 Compounds of Groups 7-3 (Mn..., Cr..., V..., Ti..., Sc..., La..., Ac...)
- 30 Acetals: O/N, S/S, S/N, and N/N and Higher Heteroatom Analogues

\* Detailed listings of product classes and subclasses, methods, and variations can be found in the **Table of Contents** sections of every volume.

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## Science of Synthesis

**Science of Synthesis** is the authoritative and comprehensive reference work for the entire field of organic and organometallic synthesis.

**Science of Synthesis** presents the important synthetic methods for all classes of compounds and includes:

- Methods critically evaluated by leading scientists
- Background information and detailed experimental procedures
- Schemes and tables which illustrate the reaction scope



# Science of Synthesis

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# Science of Synthesis

## Knowledge Updates 2016/2

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## Preface

As the pace and breadth of research intensifies, organic synthesis is playing an increasingly central role in the discovery process within all imaginable areas of science: from pharmaceuticals, agrochemicals, and materials science to areas of biology and physics, the most impactful investigations are becoming more and more molecular. As an enabling science, synthetic organic chemistry is uniquely poised to provide access to compounds with exciting and valuable new properties. Organic molecules of extreme complexity can, given expert knowledge, be prepared with exquisite efficiency and selectivity, allowing virtually any phenomenon to be probed at levels never before imagined. With ready access to materials of remarkable structural diversity, critical studies can be conducted that reveal the intimate workings of chemical, biological, or physical processes with stunning detail.

The sheer variety of chemical structural space required for these investigations and the design elements necessary to assemble molecular targets of increasing intricacy place extraordinary demands on the individual synthetic methods used. They must be robust and provide reliably high yields on both small and large scales, have broad applicability, and exhibit high selectivity. Increasingly, synthetic approaches to organic molecules must take into account environmental sustainability. Thus, atom economy and the overall environmental impact of the transformations are taking on increased importance.

The need to provide a dependable source of information on evaluated synthetic methods in organic chemistry embracing these characteristics was first acknowledged over 100 years ago, when the highly regarded reference source **Houben–Weyl Methoden der Organischen Chemie** was first introduced. Recognizing the necessity to provide a modernized, comprehensive, and critical assessment of synthetic organic chemistry, in 2000 Thieme launched **Science of Synthesis, Houben–Weyl Methods of Molecular Transformations**. This effort, assembled by almost 1000 leading experts from both industry and academia, provides a balanced and critical analysis of the entire literature from the early 1800s until the year of publication. The accompanying online version of **Science of Synthesis** provides text, structure, substructure, and reaction searching capabilities by a powerful, yet easy-to-use, intuitive interface.

From 2010 onward, **Science of Synthesis** is being updated quarterly with high-quality content via **Science of Synthesis Knowledge Updates**. The goal of the **Science of Synthesis Knowledge Updates** is to provide a continuous review of the field of synthetic organic chemistry, with an eye toward evaluating and analyzing significant new developments in synthetic methods. A list of stringent criteria for inclusion of each synthetic transformation ensures that only the best and most reliable synthetic methods are incorporated. These efforts guarantee that **Science of Synthesis** will continue to be the most up-to-date electronic database available for the documentation of validated synthetic methods.

Also from 2010, **Science of Synthesis** includes the **Science of Synthesis Reference Library**, comprising volumes covering special topics of organic chemistry in a modular fashion, with six main classifications: (1) Classical, (2) Advances, (3) Transformations, (4) Applications, (5) Structures, and (6) Techniques. Titles will include *Stereoselective Synthesis*, *Water in Organic Synthesis*, and *Asymmetric Organocatalysis*, among others. With expert-evaluated content focusing on subjects of particular current interest, the **Science of Synthesis Reference Library** complements the **Science of Synthesis Knowledge Updates**, to make **Science of Synthesis** the complete information source for the modern synthetic chemist.

The overarching goal of the **Science of Synthesis** Editorial Board is to make the suite of **Science of Synthesis** resources the first and foremost focal point for critically evaluated information on chemical transformations for those individuals involved in the design and construction of organic molecules.

Throughout the years, the chemical community has benefited tremendously from the outstanding contribution of hundreds of highly dedicated expert authors who have devoted their energies and intellectual capital to these projects. We thank all of these individuals for the heroic efforts they have made throughout the entire publication process to make **Science of Synthesis** a reference work of the highest integrity and quality.

### **The Editorial Board**

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## Abstracts

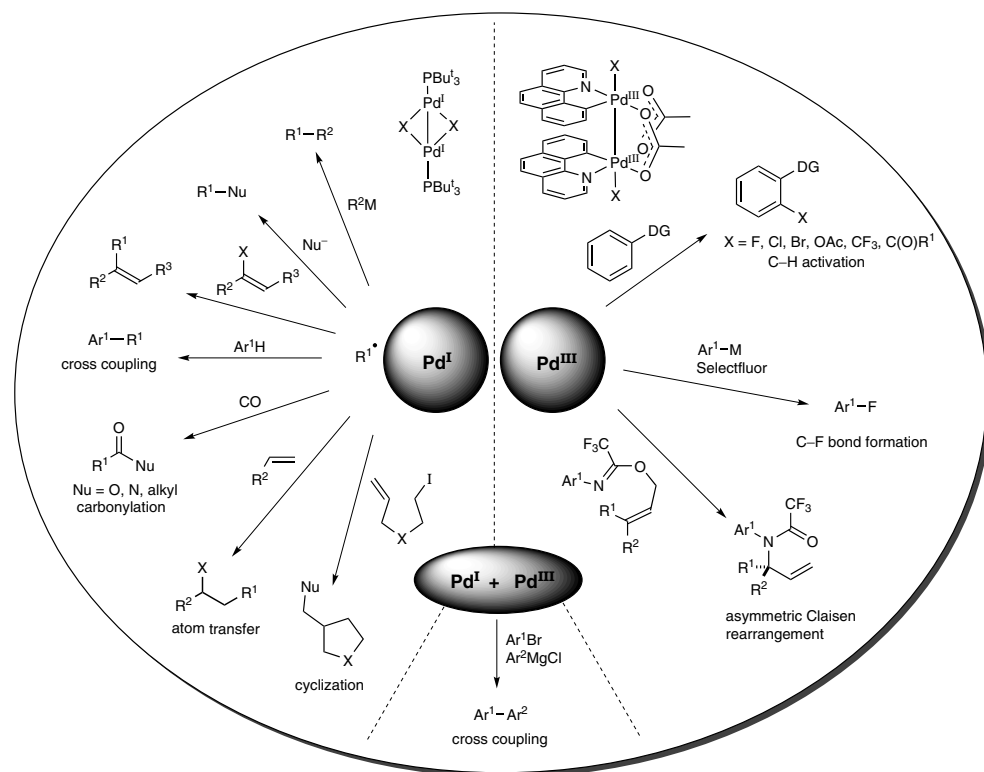
New

p 1

### 1.2.7 Radical-Based Palladium-Catalyzed Bond Constructions

*Y. Li, W. Xie, and X. Jiang*

Palladium(0) and palladium(II) species are frequently used as catalysts and are considered to be active intermediates in traditional palladium-catalyzed coupling reactions, participating in oxidative addition and reductive elimination via two-electron-transfer processes. Meanwhile, the catalytic modes involving palladium(I) and palladium(III) have been gradually developed. Single-electron-transfer pathways are thought to be involved via related catalytic cycles. Various palladium(I) and palladium(III) complexes have been synthesized and characterized. The palladium(I) precatalysts in Suzuki coupling and Buchwald–Hartwig amination exhibit higher reactivity than traditional palladium(0) and palladium(II) catalysts. Palladium-catalyzed single-electron-transfer conditions allow alkyl halides to participate in a series of cross-coupling, carbonylation, atom-transfer, and cyclization reactions, in which the palladium(I) species and various alkyl radicals are thought to be key intermediates. Palladium(III) species have been proposed as active intermediates in various directed C–H activation reactions. Moreover, it has been proved that palladium(III) intermediates can catalyze C–F bond formation and asymmetric Claisen rearrangement reactions. Beyond these systems, it is thought that palladium(I) and palladium(III) species might take part in the same system. In summary, radical-type palladium-catalyzed systems possess new properties which help to realize various otherwise difficult transformations.



**Keywords:** bond construction · palladium(I) catalysis · palladium(III) catalysis · radical processes

New

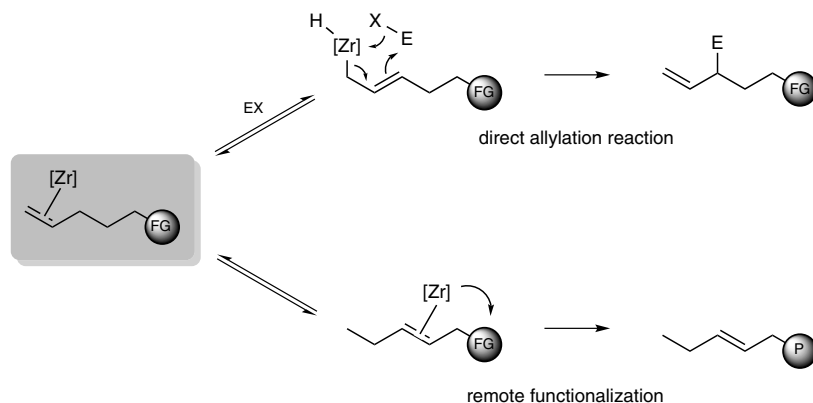
p 113

2.11.15 **C(sp<sup>3</sup>)-H Functionalization by Allylic C-H Activation of Zirconocene Complexes**

A. Vasseur and J. Bruffaerts

Zirconocene-assisted allylic C(sp<sup>3</sup>)-H activation allows the remote functionalization of alkenes through multipositional migration of the olefinic double bond as a communicative process between two distant sites. The transformation involves the successive formation of zirconacyclopropane species along an alkyl chain. This C-H activation promoted migration proceeds rapidly under mild conditions. Moreover, it occurs in a unidirectional manner if associated with thermodynamically favored termination steps such as elimination, selective carbon-carbon bond activation, or ring expansion. The remotely formed zirconocene species can subsequently react with a variety of electrophilic carbon, oxygen, or nitrogen reagents to give a wide range of added-value products from simple substrates. Transmetalation processes further increase the synthetic potential by allowing the remote formation of a new carbon-carbon bond. The global transformation is not

only stereo- and regioselective, but also enables the relay of stereochemical information. Alternatively, a zirconacyclopropane/crotylzirconocene hydride equilibrium can be promoted under particular reaction conditions, leading to direct regio- and stereoselective allylation reactions with acid chloride, aldehyde, diketone and imine derivatives.



**Keywords:** zirconocenes · allylic C–H activation · alkenes · conjugated dienes · trienes · homoallylic alcohols · homoallylic amines · alkenylcyclopropanes · cyclopropanols · diastereoselectivity · quaternary stereocenters

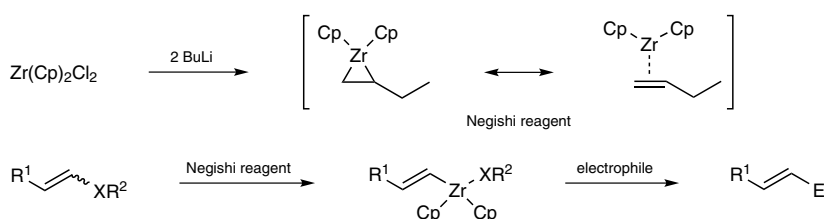
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## 2.11.16 Synthesis and Reactivity of Heteroatom-Substituted Vinylzirconocene Derivatives and Hetarylzirconocenes

*J. Bruffaerts and A. Vasseur*

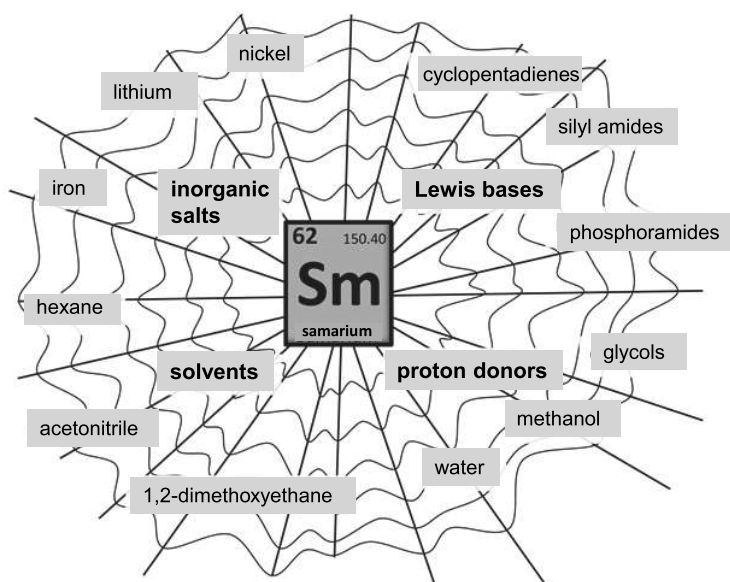
Reactive and stereodefined vinylzirconocene derivatives are efficiently prepared from a variety of different heterosubstituted alkenes in the presence of a stoichiometric amount of the Negishi reagent. This chapter describes the synthesis of these compounds along with their applications in the synthesis of various substituted alkenes.



**Keywords:** organometallic compounds · zirconocenes · alkenes · vinyl compounds · stereoselective synthesis · elimination

**2.12.17 The Role of Solvents and Additives in Reactions of Samarium(II) Iodide and Related Reductants***T. V. Chciuk and R. A. Flowers, II*

The use of additives with samarium(II) iodide ( $\text{SmI}_2$ ) greatly impacts the rate, diastereoselectivity, and chemoselectivity of its reactions. Additives that are commonly utilized with samarium(II) iodide and other samarium(II)-based reductants can be classified into three major groups: (1) Lewis bases such as hexamethylphosphoric triamide (HMPA) and other electron-donor ligands and chelating ethers; (2) proton donors, such as water, alcohols, and glycols; and (3) inorganic additives such as nickel(II) iodide, iron(III) chloride, and lithium chloride. In addition, the solvent milieu can also play an important role in the reactivity of samarium(II) reductants, predominantly through changes in the coordination sphere of the metal. The main focus of this chapter is on the use of additives and solvent milieu to provide selective and efficient reactions, with at least one example being given for each subclass of samarium(II)-promoted reaction.



**Keywords:** cross-coupling reactions · electron transfer · hexamethylphosphoric triamide · inorganic additives · intramolecular cyclization · Lewis bases · proton donors · reductive coupling · ring expansion · samarium(II) iodide · solvent effects

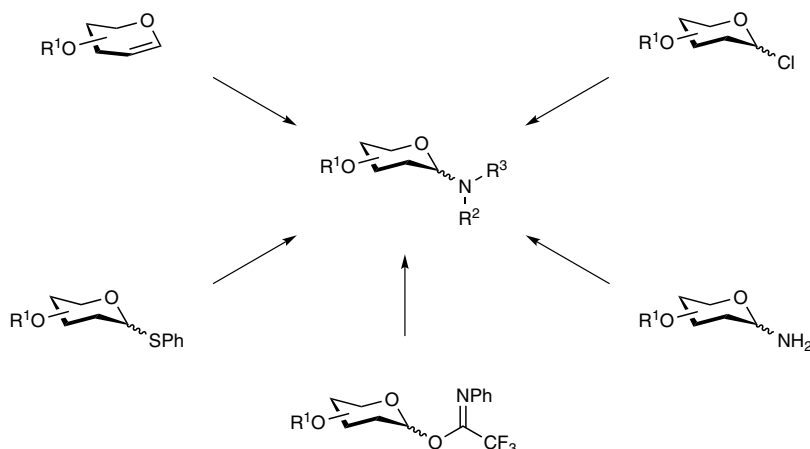
2016

p 267

## 30.1.3 Carbohydrate Derivatives (Including Nucleosides)

T. Nokami

*O,N*-Acetals are found in various types of organic molecules and are core motifs in carbohydrates, including nucleosides. This chapter summarizes the synthetic methods to prepare *N*-linked glycopeptides, ribonucleosides, 2-deoxyribonucleosides, and others. Glycosylation between the anomeric carbon and the nitrogen atom of a nucleophile is a conventional method for the synthesis of these molecules, but stereoselectivity highly depends on the structures of the substrates. Glycosylamines are also important precursors for the stereoselective synthesis of *N*-linked glycopeptides and ribonucleosides.



**Keywords:** aminoglycosides · carbohydrates · glycopeptides · glycosylation · nucleosides

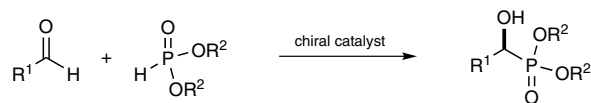
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p 295

30.2.3 *O,P*-Acetals

K. Murai and H. Fujioka

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.2) describing methods for the synthesis of *O,P*-acetals. It focuses on the literature published in the period 2006–2015. Key methods covered include the addition of phosphorus compounds to carbonyl groups (including enantioselective variations), kinetic resolution of  $\alpha$ -hydroxyphosphonates, oxidation of  $\alpha,\beta$ -unsaturated phosphorus compounds, addition of phosphorus compounds to *O,O*-acetals, reduction of acylphosphonates and related compounds, and aldol-type reactions of keto phosphonates.



**Keywords:** *O,P*-acetals · asymmetric synthesis · diastereoselectivity · enantioselectivity · kinetic resolution · hydrogenation · organocatalysis · oxidation · epoxidation · reduction · phosphorus compounds · Pudovik reaction

2016

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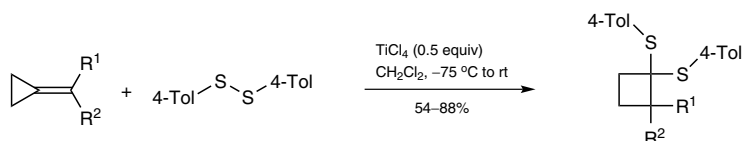
2016

p 329

30.3.1.3 **Acyclic S,S-Acetals**

A. Tsubouchi

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.3.1) describing methods for the preparation of acyclic S,S-acetals. It focuses on the literature published in the period 2006–2014, presenting complementary information with respect to new developments and transformations. It also contains an important extension of the coverage of the previous contribution. Key methods covered include the thioacetalization of carbonyl compounds using a variety of catalysts, conversion of O,O-acetals, addition of thiols to C=C multiple bonds, addition of disulfides to methylenecyclopropanes, and ring opening of 1,2-cyclopropanated 3-oxo sugars with thiols.



**Keywords:** acetals · carbonyl compounds · chemoselectivity · Lewis acid catalysts · S,S-acetals · supported catalysis · surfactants · thiols · ring opening

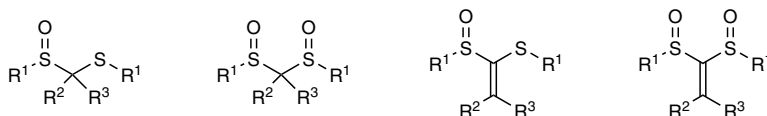
2016

p 351

30.3.6.3 **Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides**

A. Ishii

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.3.6) published in 2007. S,S-Acetal S-oxides and S,S'-dioxides are synthesized by the reaction of sulfanyl- or sulfinyl-stabilized carbanions with electrophiles or by the (asymmetric) oxidation of S,S-acetals. Reaction of a carbanion with an aldehyde or ketone followed by dehydration provides ketene S,S-acetal oxides. Recent advances in synthetic application have been seen in conjugate additions of nucleophiles or radicals to ketene S,S-acetal oxides and in reactions utilizing reactive sulfonium intermediates generated by treatment with acid anhydrides (Pummerer conditions).



**Keywords:** sulfur-stabilized carbanions · asymmetric oxidation · condensation · ketene dithioacetals · conjugate addition · cyclopropanation · cross-coupling reaction · hydrolysis · Pummerer conditions · benzo[b]chalcogenophenes

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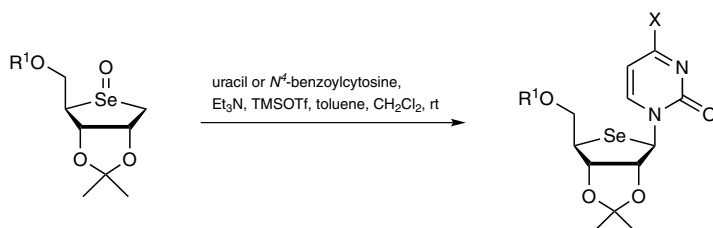
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p 379

30.5.6 **Selenium- and Tellurium-Containing Acetals**

M. Yoshimatsu

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.5) concerning the synthesis and reactions of selenium- and tellurium-containing acetals. Recent interest has changed to the new field of *Se,N*- and *Te,N*-acetals including 4'-selenonucleosides, which may be used as unique building blocks for new DNA and RNA analogues. The published methods for *Se,N*- and *Te,N*-acetals could open up new applications in this field.



**Keywords:** *Se,Se*-acetals · *Se,Te*-acetals · *Se,N*-acetals · 4'-selenonucleosides · seleno-Pummerer reactions

2016

p 407

30.7.3 ***N,P*- and *P,P*-Acetals**

T. Kimura

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.7) describing methods for the synthesis of *N,P*- and *P,P*-acetals. It focuses on the literature published in the period 2007–2014. As well as covering the synthesis of the title compounds, their applications in organic synthesis are also briefly reviewed.



**Keywords:**  $\alpha$ -aminophosphonates · hydrophosphorylation · imines · Pudovik addition · Kabachnik–Fields three-component condensation · Horner–Wadsworth–Emmons alkenation · *gem*-bisphosphonates · phospho-Claisen condensation · Michaelis–Becker substitution · Michaelis–Arbuzov rearrangement

2016

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## Science of Synthesis Knowledge Updates 2016/2

	<b>Preface</b> .....	V
	<b>Abstracts</b> .....	VII
	<b>Table of Contents</b> .....	XVII
1.2.7	<b>Radical-Based Palladium-Catalyzed Bond Constructions</b> Y. Li, W. Xie, and X. Jiang .....	1
2.11.15	<b>C(sp<sup>3</sup>)—H Functionalization by Allylic C—H Activation of Zirconocene Complexes</b> A. Vasseur and J. Bruffaerts .....	113
2.11.16	<b>Synthesis and Reactivity of Heteroatom-Substituted Vinylzirconocene Derivatives and Hetarylzirconocenes</b> J. Bruffaerts and A. Vasseur .....	147
2.12.17	<b>The Role of Solvents and Additives in Reactions of Samarium(II) Iodide and Related Reductants</b> T. V. Chciuk and R. A. Flowers, II .....	177
30.1.3	<b>Carbohydrate Derivatives (Including Nucleosides)</b> T. Nokami .....	267
30.2.3	<b>O,P-Acetals (Update 2016)</b> K. Murai and H. Fujioka .....	295
30.3.1.3	<b>Acyclic S,S-Acetals (Update 2016)</b> A. Tsubouchi .....	329
30.3.6.3	<b>Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides (Update 2016)</b> A. Ishii .....	351
30.5.6	<b>Selenium- and Tellurium-Containing Acetals (Update 2016)</b> M. Yoshimatsu .....	379
30.7.3	<b>N,P- and P,P-Acetals (Update 2016)</b> T. Kimura .....	407
	<b>Author Index</b> .....	463
	<b>Abbreviations</b> .....	479



## Table of Contents

### Volume 1: Compounds with Transition Metal–Carbon $\pi$ -Bonds and Compounds of Groups 10–8 (Ni, Pd, Pt, Co, Rh, Ir, Fe, Ru, Os)

1.2	<b>Product Class 2: Organometallic Complexes of Palladium</b>		
1.2.7	<b>Radical-Based Palladium-Catalyzed Bond Constructions</b>		(New)
	Y. Li, W. Xie, and X. Jiang		
1.2.7	<b>Radical-Based Palladium-Catalyzed Bond Constructions</b>	.....	1
1.2.7.1	Method 1: Reactions Involving Palladium(I) Species	.....	1
1.2.7.1.1	Variation 1: Synthesis of Organometallic Palladium(I) Complexes	.....	1
1.2.7.1.2	Variation 2: Reactions Involving Palladium(I) Precatalysts	.....	8
1.2.7.1.3	Variation 3: Cross-Coupling Reactions	.....	16
1.2.7.1.4	Variation 4: Carbonylation Reactions	.....	27
1.2.7.1.5	Variation 5: Cyclization Reactions	.....	42
1.2.7.1.6	Variation 6: Atom-Transfer Reactions	.....	48
1.2.7.2	Method 2: Reactions Involving Palladium(III) Species	.....	62
1.2.7.2.1	Variation 1: Synthesis of Organometallic Palladium(III) Complexes	.....	62
1.2.7.2.2	Variation 2: C–H Activation Reactions Involving Palladium(III)	.....	72
1.2.7.2.3	Variation 3: C–F Bond-Constructing Reactions Involving Palladium(III)	...	79
1.2.7.2.4	Variation 4: Reactions Involving Phenyl or Benzoyl Radicals	.....	82
1.2.7.2.5	Variation 5: Asymmetric Aza-Claisen Rearrangements	.....	92
1.2.7.3	Method 3: Reactions Involving Palladium(I) and Palladium(III) Species	..	95
1.2.7.4	Method 4: Miscellaneous Reactions	.....	98

## Volume 2: Compounds of Groups 7–3 (Mn..., Cr..., V..., Ti..., Sc..., La..., Ac...)

2.11	<b>Product Class 11: Organometallic Complexes of Zirconium and Hafnium</b>	
2.11.15	<b>C(sp<sup>3</sup>)—H Functionalization by Allylic C—H Activation of Zirconocene Complexes</b>	(New)
	A. Vasseur and J. Bruffaerts	
2.11.15	<b>C(sp<sup>3</sup>)—H Functionalization by Allylic C—H Activation of Zirconocene Complexes</b>	113
2.11.15.1	Method 1: Synthesis of Conjugated Dienes from Nonconjugated Dienes	118
2.11.15.1.1	Variation 1: From Nonheteroatom-Substituted Alkenes	118
2.11.15.1.2	Variation 2: From Nonconjugated Dienes Bearing an Alkoxy Substituent	119
2.11.15.2	Method 2: Synthesis of Trienes	122
2.11.15.3	Method 3: Synthesis of Homoallylic Alcohols	123
2.11.15.3.1	Variation 1: From Acid Chlorides without Ligand Exchange	123
2.11.15.3.2	Variation 2: From Acid Chlorides with Ligand Exchange	124
2.11.15.3.3	Variation 3: From Aldehydes without Ligand Exchange	126
2.11.15.3.4	Variation 4: From Aldehydes with Ligand Exchange	128
2.11.15.4	Method 4: Diastereoselective Synthesis of Homoallylic Amines	129
2.11.15.5	Method 5: Diastereoselective Synthesis of 1,4-Homoallylic Diols	130
2.11.15.5.1	Variation 1: From Grignard Reagents	130
2.11.15.5.2	Variation 2: From Terminal Alkenes	132
2.11.15.6	Method 6: Synthesis of 1,2-Disubstituted Cyclopropanols	133
2.11.15.7	Method 7: Synthesis of Substituted Allylic Derivatives from Unsaturated Fatty Alcohols	133
2.11.15.8	Method 8: Selective Reduction of the Double Bond of $\omega$ -Ene Dihydrofurans and Dihydropyrans	135
2.11.15.9	Method 9: Synthesis of Acyclic Fragments Possessing an All-Carbon Quaternary Stereogenic Center	136
2.11.15.9.1	Variation 1: From $\omega$ -Ene Cyclopropanes	136
2.11.15.9.2	Variation 2: From Alkylidenecyclopropanes	139
2.11.15.9.3	Variation 3: From $\omega$ -Alkenylcyclopropanes Bearing a Leaving Group	142

2.11.16	<b>Synthesis and Reactivity of Heteroatom-Substituted Vinylzirconocene Derivatives and Hetarylzirconocenes</b>	New
	J. Bruffaerts and A. Vasseur	
<hr/>		
2.11.16	<b>Synthesis and Reactivity of Heteroatom-Substituted Vinylzirconocene Derivatives and Hetarylzirconocenes</b> .....	147
2.11.16.1	General Preparation of Vinylzirconocene Derivatives .....	148
2.11.16.2	General Reactivity of Vinylzirconocene Derivatives .....	150
2.11.16.3	Preparation of Vinylzirconocene Derivatives from Heteroatom-Substituted Alkenes .....	151
2.11.16.3.1	Method 1: From Alkenyl Halides .....	152
2.11.16.3.2	Method 2: From Aryl Halides .....	154
2.11.16.3.3	Method 3: From Enol Sulfonates .....	158
2.11.16.3.4	Method 4: From Enol Ethers and Silyl Enol Ethers .....	160
2.11.16.3.5	Method 5: From Sulfides, Sulfoxides, and Sulfones .....	162
2.11.16.3.6	Method 6: From Carbamates .....	166
2.11.16.3.7	Method 7: From Dienyl Systems .....	168
2.12	<b>Product Class 12: Organometallic Complexes of Scandium, Yttrium, and the Lanthanides</b>	
<hr/>		
2.12.17	<b>The Role of Solvents and Additives in Reactions of Samarium(II) Iodide and Related Reductants</b>	New
	T. V. Chciuk and R. A. Flowers, II	
<hr/>		
2.12.17	<b>The Role of Solvents and Additives in Reactions of Samarium(II) Iodide and Related Reductants</b> .....	177
2.12.17.1	Synthesis of Samarium(II) Reductants .....	177
2.12.17.1.1	Samarium(II) Iodide .....	178
2.12.17.1.1.1	Method 1: Synthesis in Tetrahydrofuran from Samarium and 1,2-Diiodoethane .....	178
2.12.17.1.1.2	Method 2: Synthesis in Tetrahydrofuran from Samarium and Iodine ....	179
2.12.17.1.1.3	Method 3: Synthesis in Tetrahydropyran .....	181
2.12.17.1.1.4	Method 4: Synthesis in 1,2-Dimethoxyethane .....	181
2.12.17.1.1.5	Method 5: Synthesis in Acetonitrile and Other Nitriles .....	181
2.12.17.1.1.6	Method 6: Synthesis in Benzene/Hexamethylphosphoric Triamide .....	183
2.12.17.1.2	Samarium(II) Bromide and Samarium(II) Chloride .....	183
2.12.17.1.2.1	Method 1: Synthesis of Samarium(II) Bromide from Samarium(III) Oxide and Hydrobromic Acid .....	184
2.12.17.1.2.2	Method 2: Synthesis of Samarium(II) Bromide from Samarium and 1,1,2,2-Tetrabromoethane .....	184
2.12.17.1.2.3	Method 3: Synthesis of Samarium(II) Bromide from Samarium(II) Iodide and Lithium Bromide .....	185

2.12.17.1.2.4	Method 4:	Synthesis of Samarium(II) Chloride from Samarium(III) Chloride .....	185
2.12.17.1.2.5	Method 5:	Synthesis of Samarium(II) Chloride from Samarium(II) Iodide and Lithium Chloride .....	186
2.12.17.1.2.6	Method 6:	Synthesis of Samarium(II) Chloride in Water from Samarium(III) Chloride and Samarium .....	186
2.12.17.1.3		Samarium(II) Trifluoromethanesulfonate .....	187
2.12.17.1.3.1	Method 1:	Synthesis from Samarium(III) Trifluoromethanesulfonate, Samarium Metal, and Ethylmagnesium Bromide .....	187
2.12.17.1.3.2	Method 2:	Synthesis from Samarium(III) Trifluoromethanesulfonate and <i>sec</i> -Butyllithium .....	187
2.12.17.1.3.3	Method 3:	Synthesis from Samarium Metal and 1,5-Dithionibicyclo[3.3.0]octane Bis(trifluoromethanesulfonate) .....	188
2.12.17.1.3.4	Method 4:	Mercury-Catalyzed Reduction of Samarium(III) Trifluoromethanesulfonate .....	189
2.12.17.1.3.5	Method 5:	Synthesis from Samarium(III) Trifluoromethanesulfonate and Samarium Metal .....	189
2.12.17.1.4		Samarium(II) Amides .....	190
2.12.17.1.5		( $\eta^5$ -Cyclopentadienyl)samarium(II) Complexes .....	190
2.12.17.1.5.1	Method 1:	Synthesis of Bis( $\eta^5$ -cyclopentadienyl)samarium(II) .....	191
2.12.17.1.5.2	Method 2:	Synthesis of Bis( $\eta^5$ -pentamethylcyclopentadienyl)samarium(II) .....	191
2.12.17.2		Use of Lewis Bases in Samarium(II)-Based Reactions .....	191
2.12.17.2.1		Hexamethylphosphoric Triamide .....	192
2.12.17.2.1.1	Method 1:	Reduction of Alkyl and Aryl Halides .....	192
2.12.17.2.1.2	Method 2:	Reduction of $\alpha$ -Oxygenated Carbonyl Compounds .....	192
2.12.17.2.1.3	Method 3:	Reduction of 4-Methylbenzoates .....	194
2.12.17.2.1.4	Method 4:	Grignard and Barbier Reactions .....	195
2.12.17.2.1.4.1	Variation 1:	Intermolecular Samarium Grignard Reactions .....	196
2.12.17.2.1.4.2	Variation 2:	Intermolecular Samarium Barbier Reactions .....	197
2.12.17.2.1.4.3	Variation 3:	Intramolecular Samarium Barbier Reactions .....	200
2.12.17.2.1.5	Method 5:	Reformatsky- and Aldol-Type Reactions .....	200
2.12.17.2.1.6	Method 6:	Halide–Alkene Coupling Reactions .....	201
2.12.17.2.1.7	Method 7:	Spirocyclization via Intramolecular Aryl Iodide Radical Addition .....	202
2.12.17.2.1.8	Method 8:	Carbonyl–Alkene Coupling .....	203
2.12.17.2.1.8.1	Variation 1:	Intramolecular Cyclization of Unactivated Alkenyl Ketones ...	203
2.12.17.2.1.8.2	Variation 2:	Sequential Intramolecular Cyclization with Intermolecular Electrophilic Addition .....	204
2.12.17.2.1.8.3	Variation 3:	Intermolecular Ketone–Allene Coupling .....	205
2.12.17.2.1.8.4	Variation 4:	Sequential Intramolecular Cyclization with Electrophilic Addition to 1 <i>H</i> -Indole Derivatives .....	205



2.12.17.2.1.9	Method 9:	Intramolecular Pinacol Coupling of Carbonyl Compounds ···	206
2.12.17.2.1.10	Method 10:	Intramolecular Pinacol-Type Coupling of Ketones and Imines ·	207
2.12.17.2.1.11	Method 11:	Tandem Epoxide-Opening/Cyclization To Afford $\gamma$ -Lactones ·	208
2.12.17.2.1.12	Method 12:	Tandem Elimination and Coupling of Aliphatic Imides with Carbonyl Compounds ···	209
2.12.17.2.1.13	Method 13:	Intermolecular and Intramolecular Reductive Dimerization ··	210
2.12.17.2.2	Additives Related to Hexamethylphosphoric Triamide ·····················		211
2.12.17.2.2.1	Method 1:	Tri(pyrrolidin-1-yl)phosphine Oxide in Reductive Coupling Reactions ···	212
2.12.17.2.2.2	Method 2:	<i>N</i> -Methyl- <i>P,P</i> -di(pyrrolidin-1-yl)phosphinic Amide in Reductive Cyclization Reactions ·······································	212
2.12.17.2.2.3	Method 3:	Hydroxylated Hexamethylphosphoric Triamide in Reductive Coupling Reactions ·······································	213
2.12.17.3	Use of Proton Donors in Samarium(II)-Based Reactions ···················		214
2.12.17.3.1	Water ···		214
2.12.17.3.1.1	Method 1:	Reduction of Alkyl Iodides ·····································	214
2.12.17.3.1.2	Method 2:	Reduction of Aromatic Carboxylic Acids, Esters, Amides, and Nitriles ···	215
2.12.17.3.1.3	Method 3:	Reduction of Azido Oligosaccharides to Amino Sugars ·······	216
2.12.17.3.1.4	Method 4:	Reduction of Six-Membered Lactones ···························	217
2.12.17.3.1.5	Method 5:	Reduction of Cyclic Esters ···································	218
2.12.17.3.1.6	Method 6:	Reductive Cyclization of Lactones ···························	219
2.12.17.3.1.7	Method 7:	Reduction of Sodium <i>S</i> -Alkyl Thiosulfates and Alkyl Thio- cyanates ···	220
2.12.17.3.1.8	Method 8:	Reduction of Cyclic 1,3-Diesters ·····························	221
2.12.17.3.1.9	Method 9:	Cross Coupling of <i>N</i> -Acylloxazolidinones to Acrylamides and Acrylates ·······································	222
2.12.17.3.1.10	Method 10:	Coupling To Produce $\alpha,\alpha$ -Disubstituted Pyrrolidin-2-yl- methanols ·······································	223
2.12.17.3.1.11	Method 11:	Reductive Coupling of Nitrones and Acrylates ·················	223
2.12.17.3.2	Water and Amines ···		224
2.12.17.3.2.1	Method 1:	Reduction of Ketones ·······································	225
2.12.17.3.2.2	Method 2:	Reduction of $\beta$ -Hydroxy Ketones ·····························	225
2.12.17.3.2.3	Method 3:	Reduction of Alkyl Halides ···································	226
2.12.17.3.2.4	Method 4:	Reduction of Double and Triple Bonds in Conjugated Alkenes ·	227
2.12.17.3.2.5	Method 5:	Deprotection of Allyl Ether Protected Alcohols ···············	228
2.12.17.3.2.6	Method 6:	Deprotection of Toluenesulfonamides ·······················	229
2.12.17.3.2.7	Method 7:	Reduction of Nitroalkanes ···································	230
2.12.17.3.2.8	Method 8:	Reductive Cleavage of Benzyl-Heteroatom Bonds ···········	231
2.12.17.3.2.9	Method 9:	Reduction of Nitriles ·····································	232
2.12.17.3.2.10	Method 10:	Reduction of Unactivated Esters ···························	233
2.12.17.3.2.11	Method 11:	Reduction of Amides to Alcohols ···························	235

2.12.17.3.2.12	Method 12:	Reduction of Carboxylic Acids to Alcohols	236
2.12.17.3.2.13	Method 13:	Intramolecular Coupling of Aryl Iodides with Alkenyl and Alkynyl Groups	237
2.12.17.3.3	Methanol		238
2.12.17.3.3.1	Method 1:	Stereoselective Reduction of $\beta$ -Hydroxy Ketones to <i>anti</i> -1,3-Diols	238
2.12.17.3.3.2	Method 2:	Reductive Cyclization of $\delta$ -Halo $\alpha,\beta$ -Unsaturated Esters	238
2.12.17.3.3.3	Method 3:	Ring Expansion of Alkyl (n + 1)-Oxobicyclo[n.1.0]alkane-1-carboxylates	239
2.12.17.3.3.4	Method 4:	Cyclization of $\gamma,\delta$ -Unsaturated Ketones To Afford <i>syn</i> -Cyclopentanols	240
2.12.17.3.4	<i>tert</i> -Butyl Alcohol		241
2.12.17.3.4.1	Method 1:	Reductive Cyclization of Carbodiimides to Indolin-2-amines	241
2.12.17.3.4.2	Method 2:	Cross Coupling of Chiral <i>N</i> -( <i>tert</i> -Butylsulfinyl)imines with Aldehydes	242
2.12.17.3.5	Glycols		243
2.12.17.3.5.1	Method 1:	Synthesis of Uracils	243
2.12.17.3.6	2-(Dimethylamino)ethanol		244
2.12.17.3.6.1	Method 1:	Reductive Ring Opening of Aziridine-2-carboxylates and Aziridine-2-carboxamides to $\beta$ -Amino Esters and Amides	244
2.12.17.3.6.2	Method 2:	Simple Functional Group Reductions Using Samarium(II) Iodide/2-(Dimethylamino)ethanol	245
2.12.17.4	Use of Inorganic Additives in Samarium(II)-Based Reactions		246
2.12.17.4.1	Transition-Metal Additives		247
2.12.17.4.1.1	Method 1:	Carbonyl–Alkene Coupling Reactions	247
2.12.17.4.1.2	Method 2:	Barbier Coupling Reactions	249
2.12.17.4.2	Lithium Halide Salts		250
2.12.17.4.2.1	Method 1:	Intramolecular Coupling of Isocyanates and Cyclic $\alpha,\beta$ -Unsaturated Ketones	250
2.12.17.4.2.2	Method 2:	Cross Coupling of Nitrones with Allenates	251
2.12.17.5	Impact of Solvents on Reactivity in Samarium-Mediated Reductions and Coupling Reactions		252
2.12.17.5.1	Coordinating Solvents (Other than Tetrahydrofuran)		252
2.12.17.5.1.1	Method 1:	Coupling of Ketones with Acid Chlorides in Tetrahydropyran	252
2.12.17.5.1.2	Method 2:	Coupling of Allylic and Benzylic Samarium Compounds with Ketones and Esters in Tetrahydropyran	253
2.12.17.5.1.3	Method 3:	Reduction of $\beta$ -Hydroxy Ketones in 1,2-Dimethoxyethane	254
2.12.17.5.1.4	Method 4:	Reductive Intramolecular Ketyl–Alkene Coupling in Acetonitrile	255
2.12.17.5.1.5	Method 5:	2,3-Wittig Rearrangement by Partial Reduction of Diallyl Acetals in Acetonitrile	256

2.12.17.5.1.6	Method 6:	Coupling of $\alpha$ -Chloro $\alpha,\beta$ -Unsaturated Aryl Ketones to Aldehydes in Acetonitrile	257
2.12.17.5.1.7	Method 7:	Coupling of Carbonyls in Pivalonitrile	257
2.12.17.5.2	Non-coordinating Solvents		259
2.12.17.5.2.1	Method 1:	Barbier-Type Coupling of Aryl Halides and Ketones in Benzene/Hexamethylphosphoric Triamide	259
2.12.17.5.2.2	Method 2:	Coupling of Iodoalkynes and Carbonyl Compounds in Benzene/Hexamethylphosphoric Triamide	260
2.12.17.5.2.3	Method 3:	Reduction of Dithioacetals to Sulfides in Benzene/Hexamethylphosphoric Triamide	261
2.12.17.5.2.4	Method 4:	Reductive Defluorination in Hexane	261

## Volume 30: Acetals: O/N, S/S, S/N, and N/N and Higher Heteroatom Analogues

### 30.1 Product Class 1: O,N-Acetals

#### 30.1.3 Carbohydrate Derivatives (Including Nucleosides)

2016

T. Nokami

30.1.3	<b>Carbohydrate Derivatives (Including Nucleosides)</b>		267
30.1.3.1	Glycosyl Asparagine Derivatives		268
30.1.3.1.1	Method 1:	Synthesis from Glycosyl Imidates	268
30.1.3.1.2	Method 2:	Synthesis from Pent-4-enyl Glycosides	270
30.1.3.1.3	Method 3:	Synthesis from Thioglycosides	271
30.1.3.1.4	Method 4:	Synthesis from Glycals	272
30.1.3.1.4.1	Variation 1:	Other C—N Bonds from Glycals	275
30.1.3.1.5	Method 5:	Synthesis from Glycosyl Halides	275
30.1.3.1.6	Method 6:	Synthesis from Glycosyl Isothiocyanates	276
30.1.3.1.7	Method 7:	Synthesis from <i>N</i> -Glycosyl Hydroxylamines	277
30.1.3.1.8	Method 8:	Synthesis from Glycosyl Azides	278
30.1.3.2	Ribonucleosides		279
30.1.3.2.1	Method 1:	Synthesis from Glycosyl Acetates	280
30.1.3.2.2	Method 2:	Synthesis from Glycosyl Halides	282
30.1.3.2.3	Method 3:	Synthesis from Glycosyl Imidates	283
30.1.3.2.4	Method 4:	Synthesis from Thioglycosides	285
30.1.3.2.5	Method 5:	Synthesis from Glycosyl 2-Alk-1-ynylbenzoates	286
30.1.3.2.6	Method 6:	Synthesis from Glycosylamines	287
30.1.3.3	2-Deoxyribonucleosides		287
30.1.3.3.1	Method 1:	Synthesis from Glycosyl Halides	287
30.1.3.3.2	Method 2:	Synthesis from Thioglycosides	288

30.1.3.4	Other Deoxyfuranosides .....	290
30.1.3.4.1	Method 1: Synthesis from Glycals .....	290
30.1.3.4.2	Method 2: Synthesis from Thioglycosides .....	291

### 30.2 Product Class 2: *O,P*- and *S,P*-Acetals

30.2.3	<b><i>O,P</i>-Acetals</b> <span style="float: right; border: 1px solid black; border-radius: 50%; padding: 2px;">2016</span>	
	K. Murai and H. Fujioka	
30.2.3	<b><i>O,P</i>-Acetals</b> .....	295
30.2.3.1	Method 1: Addition of Phosphorus Compounds to Ketones or Aldehydes	295
30.2.3.1.1	Variation 1: Diastereoselective Hydrophosphonylation .....	301
30.2.3.1.2	Variation 2: Enantioselective, Metal-Catalyzed Addition of Phosphites to Aldehydes (Pudovik Reaction) .....	303
30.2.3.1.3	Variation 3: Enantioselective, Organocatalyzed Addition of Phosphites to Aldehydes (Pudovik Reaction) .....	307
30.2.3.1.4	Variation 4: Enantioselective, Metal-Catalyzed Addition of Phosphites to Ketones (Pudovik Reaction) .....	311
30.2.3.1.5	Variation 5: Enantioselective, Organocatalyzed Addition of Phosphites to Ketones (Pudovik Reaction) .....	312
30.2.3.2	Method 2: Kinetic Resolution of $\alpha$ -Hydroxy Phosphonates .....	313
30.2.3.3	Method 3: Oxidation of $\alpha,\beta$ -Unsaturated Phosphorus Compounds .....	314
30.2.3.4	Method 4: Addition of Phosphorus Compounds to <i>O,O</i> -Acetals .....	315
30.2.3.5	Method 5: Reduction/Hydrogenation .....	316
30.2.3.6	Method 6: Aldol-Type Reactions and Other Reactions Using Carbon Nucleophiles .....	320

### 30.3 Product Class 3: *S,S*-Acetals

30.3.1.3	<b>Acyclic <i>S,S</i>-Acetals</b> <span style="float: right; border: 1px solid black; border-radius: 50%; padding: 2px;">2016</span>	
	A. Tsubouchi	
30.3.1.3	<b>Acyclic <i>S,S</i>-Acetals</b> .....	329
30.3.1.3.1	Method 1: Thioacetalization of Carbonyl Compounds .....	329
30.3.1.3.1.1	Variation 1: With Metal Salt Based Lewis Acid Catalysts .....	329
30.3.1.3.1.2	Variation 2: With Non-Metal Lewis Acid Catalysts .....	333
30.3.1.3.1.3	Variation 3: With Solid-Supported Lewis Acid Catalysts .....	335
30.3.1.3.1.4	Variation 4: With Solid Acid Catalysts .....	338
30.3.1.3.1.5	Variation 5: In Micelles .....	340
30.3.1.3.1.6	Variation 6: Without Acid Catalysis .....	340
30.3.1.3.2	Method 2: Conversion of <i>O,O</i> -Acetals .....	341
30.3.1.3.2.1	Variation 1: In Micelles .....	341
30.3.1.3.2.2	Variation 2: With Odorless Thiol Equivalents .....	342

30.3.1.3.3	Method 3:	Addition of Thiols to C—C Multiple Bonds	343
30.3.1.3.3.1	Variation 1:	Addition to Propargyl Alcohols	343
30.3.1.3.3.2	Variation 2:	Addition to Allenes	344
30.3.1.3.3.3	Variation 3:	Addition to Alkynes	345
30.3.1.3.4	Method 4:	Addition of Disulfides to Methylene-cyclopropanes	347
30.3.1.3.5	Method 5:	Ring Opening of 1,2-Cyclopropanated 3-Oxo Sugars with Thiols	348
30.3.6.3	<b>Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides</b>		<b>2016</b>
	A. Ishii		
30.3.6.3	<b>Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides</b>		351
30.3.6.3.1	Synthesis of Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides		351
30.3.6.3.1.1	Method 1:	Reactions of $\alpha$ -Sulfanyl $\alpha$ -Sulfinyl Carbanions	351
30.3.6.3.1.1.1	Variation 1:	Monoalkylation with Alkyl or Hetaryl Halides, Epoxides, or Enones	351
30.3.6.3.1.1.2	Variation 2:	Condensation with Carbonyl Compounds	352
30.3.6.3.1.2	Method 2:	Oxidation Reactions	354
30.3.6.3.1.2.1	Variation 1:	Oxidation of S,S-Acetals	354
30.3.6.3.1.2.2	Variation 2:	Oxidation of Ketene S,S-Acetals	356
30.3.6.3.1.2.3	Variation 3:	Oxidation of $\alpha$ -Sulfanyl Vinyl Sulfenates	358
30.3.6.3.1.3	Method 3:	Addition of S,S-Acetal S,S'-Dioxides to Carbonyl Compounds	360
30.3.6.3.1.4	Method 4:	Conjugate Addition to Ketene S,S-Acetal S-Oxides and S,S'-Dioxides	361
30.3.6.3.1.6	Method 6:	Cross-Coupling of Ketene S,S-Acetal S-Oxides	366
30.3.6.3.2	Applications of Acyclic and Cyclic S,S-Acetal S-Oxides and S,S'-Dioxides in Organic Synthesis		367
30.3.6.3.2.1	Method 1:	Synthesis of Aldehydes from S,S-Acetal S,S'-Dioxides	367
30.3.6.3.2.2	Method 2:	Synthesis of Carboxylic Acid Derivatives from S,S-Acetal S,S'-Dioxides	368
30.3.6.3.2.3	Method 3:	Synthesis of $\alpha$ -Amino Acid Derivatives	370
30.3.6.3.2.4	Method 4:	Synthesis of Heteroaromatic Compounds	371
30.3.6.3.2.5	Method 5:	Miscellaneous Reactions of S,S-Acetal S-Oxides and S,S-Acetal S,S'-Dioxides	374

30.5	<b>Product Class 5: Selenium- and Tellurium-Containing Acetals</b>	
30.5.6	<b>Selenium- and Tellurium-Containing Acetals</b>	2016
	M. Yoshimatsu	
30.5.6	<b>Selenium- and Tellurium-Containing Acetals</b>	379
30.5.6.1	<i>S,Se-</i> and <i>S,Te-</i> Acetals	379
30.5.6.1.1	Method 1: Reaction between Selenium Dihalides and Divinyl Sulfide or Divinyl Sulfone	379
30.5.6.1.2	Method 2: Selanylation–Deselanylation Process To Introduce a C=C Bond	380
30.5.6.1.3	Method 3: Electrochemical Fluoroselanylation of Vinyl Sulfones	381
30.5.6.2	<i>Se,Se-</i> and <i>Se,Te-</i> Acetals	382
30.5.6.2.1	Method 1: Palladium-Catalyzed Double Hydroselanylation of Alkynes	382
30.5.6.2.2	Method 2: Lewis Acid Catalyzed Conversion of Methylenecyclopropanes into 1,1-Bis(organo-selanyl)cyclobutanes	383
30.5.6.2.3	Method 3: Indium/Chlorotrimethylsilane Promoted Selenoacetalization of Aldehydes Using Diorganyl Diselenides	384
30.5.6.2.4	Method 4: Diselanylation of Dihaloalkanes with 1-(Organo-selanyl)per-fluoroalkanols	384
30.5.6.2.5	Method 5: Diselanylation of Dihaloalkanes Using Selenolate Anions	385
30.5.6.3	<i>Te,Te-</i> Acetals	386
30.5.6.3.1	Method 1: In Situ Generation and Reaction of Tellurocarbmates with Dihaloalkanes	386
30.5.6.4	<i>Se,N-</i> Acetals	387
30.5.6.4.1	Method 1: Phosphoric Acid Catalyzed Addition of Benzeneselenol to an <i>N</i> -Acylimine	387
30.5.6.4.2	Method 2: 1,3-Dipolar Cycloaddition Reactions between Azidomethyl Aryl Selenides and Alkynes (Click Reactions)	387
30.5.6.4.3	Method 3: Base-Promoted Selanylation Using <i>Se</i> -[2-(Trimethylsilyl)ethyl] 4-Methylbenzoselenoate	389
30.5.6.4.4	Method 4: Synthesis of 4'-Selenonucleosides by Pummerer Condensation	390
30.5.6.4.5	Method 5: Synthesis of 3'-Azido-4'-selenonucleosides and Related Derivatives	394
30.5.6.4.6	Method 6: [2 + 2] Cyclization of <i>S,Se</i> -Diphenyl Carbonimidoseleothioates with Ketene Equivalents	396
30.5.6.4.7	Method 7: Reactions of Selenoamide Dianions with <i>N,N</i> -Disubstituted Thio- or Selenoformamides	397
30.5.6.4.8	Method 8: Photoinduced Di- $\pi$ -methane Rearrangement of 3-(Organo-selanyl)-5 <i>H</i> -2,5-methanobenzo[ <i>f</i> ][1,2]thiazepine 1,1-Dioxide	398
30.5.6.4.9	Method 9: Decarboxylative Selanylation of Acids	398
30.5.6.4.10	Method 10: Base-Promoted Alkylation of $\alpha$ -Selanyl Nitroalkanes	399

30.5.6.4.11	Method 11:	Reaction of Bromoalkanes with Selenium/Sodium Borohydride	399
30.5.6.4.12	Method 12:	Selanylation of (Chloromethyl)benzotriazoles	400
30.5.6.4.13	Method 13:	Synthesis of (Arylselanyl)methyl-Functionalized Imidazolium Ionic Liquids	400
30.5.6.4.14	Method 14:	Application of <i>N</i> -[(Phenylselanyl)methyl]phthalimide as a Reagent for Protecting Alcohols as Phthalimidomethyl Ethers	400
30.5.6.5		<i>Se,P</i> - and <i>Te,P</i> -Acetals	401
30.5.6.5.1	Method 1:	Diels–Alder Reaction of Selenoaldehydes and Phosphole Chalcogenides	401
30.5.6.5.2	Method 2:	Michaelis–Arbuzov Reaction of Chloromethyl Phenyl Selenide	402
30.5.6.5.3	Method 3:	Reaction between a Phosphorylmethyl 4-Toluenesulfonate and Sodium Selenide or Telluride	402
30.5.6.5.4	Method 4:	Base-Promoted Reaction between Bis[(diphenylphosphoryl)methyl] Telluride and Chalcones	403

### 30.7 Product Class 7: *N,P*- and *P,P*-Acetals

#### 30.7.3 *N,P*- and *P,P*-Acetals

2016

T. Kimura

30.7.3	<b><i>N,P</i>- and <i>P,P</i>-Acetals</b>	407
30.7.3.1	<i>N,P</i> -Acetals	407
30.7.3.1.1	Synthesis of <i>N,P</i> -Acetals	407
30.7.3.1.1.1	Method 1: Cross Dehydrogenative Coupling of Amines and Phosphonates	407
30.7.3.1.1.1.1	Variation 1: Using a Copper Catalyst under an Oxygen Atmosphere	408
30.7.3.1.1.1.2	Variation 2: Using an Iron Catalyst and <i>tert</i> -Butyl Hydroperoxide as Co-oxidant	408
30.7.3.1.1.2	Method 2: Aldehyde-Induced C–H Substitution with Phosphine Oxides	409
30.7.3.1.1.3	Method 3: Electrophilic Amination	410
30.7.3.1.1.4	Method 4: Aldehyde-Induced Decarboxylative Coupling of $\alpha$ -Amino Acids and Phosphonates	411
30.7.3.1.1.4.1	Variation 1: Using Copper/ <i>N,N</i> -Diisopropylethylamine Catalyst	412
30.7.3.1.1.4.2	Variation 2: Without Catalyst	413
30.7.3.1.1.5	Method 5: Substitution of $\alpha$ -Hydroxyphosphonates with Amines	413
30.7.3.1.1.5.1	Variation 1: Under Microwave Irradiation	414
30.7.3.1.1.5.2	Variation 2: Using Trifluoromethanesulfonic Acid	414
30.7.3.1.1.6	Method 6: Substitution of $\alpha$ -Amido Sulfones with Organophosphorus Compounds	415
30.7.3.1.1.7	Method 7: Substitution of Dichloromethane with Tertiary Amines and Organophosphorus Compounds	416
30.7.3.1.1.8	Method 8: Asymmetric Hydrogenation of $\alpha$ -Enamido Phosphonates	417

30.7.3.1.1.9	Method 9:	Reduction of $\alpha$ -Iminophosphonates	418
30.7.3.1.1.10	Method 10:	1,4-Addition of Aryltrifluoroborates to $\alpha$ -Enamido Phosphonates	419
30.7.3.1.1.11	Method 11:	Addition of Carbon Nucleophiles to $\alpha$ -Iminophosphonates	420
30.7.3.1.1.11.1	Variation 1:	Using Terminal Alkynes	420
30.7.3.1.1.11.2	Variation 2:	Using Pyruvonnitrile	421
30.7.3.1.1.12	Method 12:	Hydrophosphorylation of Imines (Pudovik Reaction)	422
30.7.3.1.1.12.1	Variation 1:	Using a Chiral Aluminum–Salalen Catalyst	423
30.7.3.1.1.12.2	Variation 2:	Using a Chiral Tethered Bis(quinolin-8-olato)aluminum Catalyst	424
30.7.3.1.1.12.3	Variation 3:	Using Cinchona Alkaloid Catalysts	425
30.7.3.1.1.12.4	Variation 4:	Using a Chiral Copper Catalyst	426
30.7.3.1.1.12.5	Variation 5:	Using a Chiral Auxiliary	427
30.7.3.1.1.13	Method 13:	Three-Component Coupling Reaction of Amines, Carbonyl Compounds, and Phosphonates (Kabachnik–Fields Reaction)	428
30.7.3.1.1.13.1	Variation 1:	Using a Magnesium Perchlorate Catalyst	428
30.7.3.1.1.13.2	Variation 2:	Using a Chiral Phosphoric Acid Catalyst	429
30.7.3.1.1.14	Method 14:	Reductive Phosphorylation of Amides	431
30.7.3.1.1.15	Method 15:	Hydroamination and Hydrophosphorylation of Alkynes	431
30.7.3.1.1.16	Method 16:	Asymmetric Isomerization of $\alpha$ -Iminophosphonates	433
30.7.3.1.1.17	Method 17:	Consecutive Reaction of Methyleneaziridines with Organo-magnesium Chlorides, Organic Bromides, and Phosphonates	434
30.7.3.1.1.18	Method 18:	Three-Component Coupling of $\alpha$ -Diazophosphonates, Anilines, and Aldehydes	435
30.7.3.1.2	Applications of <i>N,P</i> -Acetals in Organic Synthesis		436
30.7.3.1.2.1	Method 1:	Horner–Wadsworth–Emmons Alkenation	436
30.7.3.1.2.2	Method 2:	Intramolecular Hydroamination of $\alpha$ -Aminophosphonates Possessing an Alkynyl Group	437
30.7.3.1.2.2.1	Variation 1:	Via 5- <i>exo-dig</i> Cyclization Using a Palladium Catalyst	438
30.7.3.1.2.2.2	Variation 2:	Via 6- <i>endo-dig</i> Cyclization Using a Silver Catalyst	438
30.7.3.1.2.3	Method 3:	[3 + 2] Cycloaddition with Alkenes	439
30.7.3.2	<i>P,P</i> -Acetals		440
30.7.3.2.1	Synthesis of <i>P,P</i> -Acetals		441
30.7.3.2.1.1	Method 1:	Consecutive Phosphorylation of Carbanions	441
30.7.3.2.1.2	Method 2:	Phosphorylation of $\alpha$ -Phosphoryl Carbanions	442
30.7.3.2.1.2.1	Variation 1:	Generated from Alkylphosphonates	442
30.7.3.2.1.2.2	Variation 2:	Via Phospha-Claisen Condensation	443
30.7.3.2.1.2.3	Variation 3:	Generated from Phosphine Sulfides	444
30.7.3.2.1.2.4	Variation 4:	Generated from Phosphine–Boranes	446
30.7.3.2.1.3	Method 3:	Synthesis from $\alpha$ -Chloroalkylphosphonates, Organoboranes, and Chlorophosphines	446
30.7.3.2.1.4	Method 4:	Substitution of $\alpha$ -Silylphosphines with Chlorophosphines	448



30.7.3.2.1.5	Method 5:	Consecutive Substitution of Dihaloalkanes with Organophosphorus Nucleophiles	449
30.7.3.2.1.5.1	Variation 1:	Using Phosphides	449
30.7.3.2.1.5.2	Variation 2:	Using Phosphites (Michaelis–Arbuzov Reaction)	451
30.7.3.2.1.6	Method 6:	Substitution of Organophosphorus Compounds Possessing a Leaving Group at the $\alpha$ -Position with Organophosphorus Nucleophiles	451
30.7.3.2.1.6.1	Variation 1:	Using Phosphides	452
30.7.3.2.1.6.2	Variation 2:	Using Phosphites (Michaelis–Arbuzov Reaction)	453
30.7.3.2.1.7	Method 7:	Conjugate Addition to Vinylidenebisphosphonates	453
30.7.3.2.1.7.1	Variation 1:	Using Aldehydes in the Presence of an Organocatalyst	454
30.7.3.2.1.7.2	Variation 2:	Using Boronic Acids in the Presence of a Copper Catalyst	454
30.7.3.2.2	Applications of <i>P,P</i> -Acetals in Organic Synthesis		455
30.7.3.2.2.1	Method 1:	Alkylation of <i>gem</i> -Bisphosphorus Compounds	455
30.7.3.2.2.2	Method 2:	Horner–Wadsworth–Emmons Alkenation	456
<b>Author Index</b>			463
<b>Abbreviations</b>			479



## 1.2.7 Radical-Based Palladium-Catalyzed Bond Constructions

Y. Li, W. Xie, and X. Jiang

### General Introduction

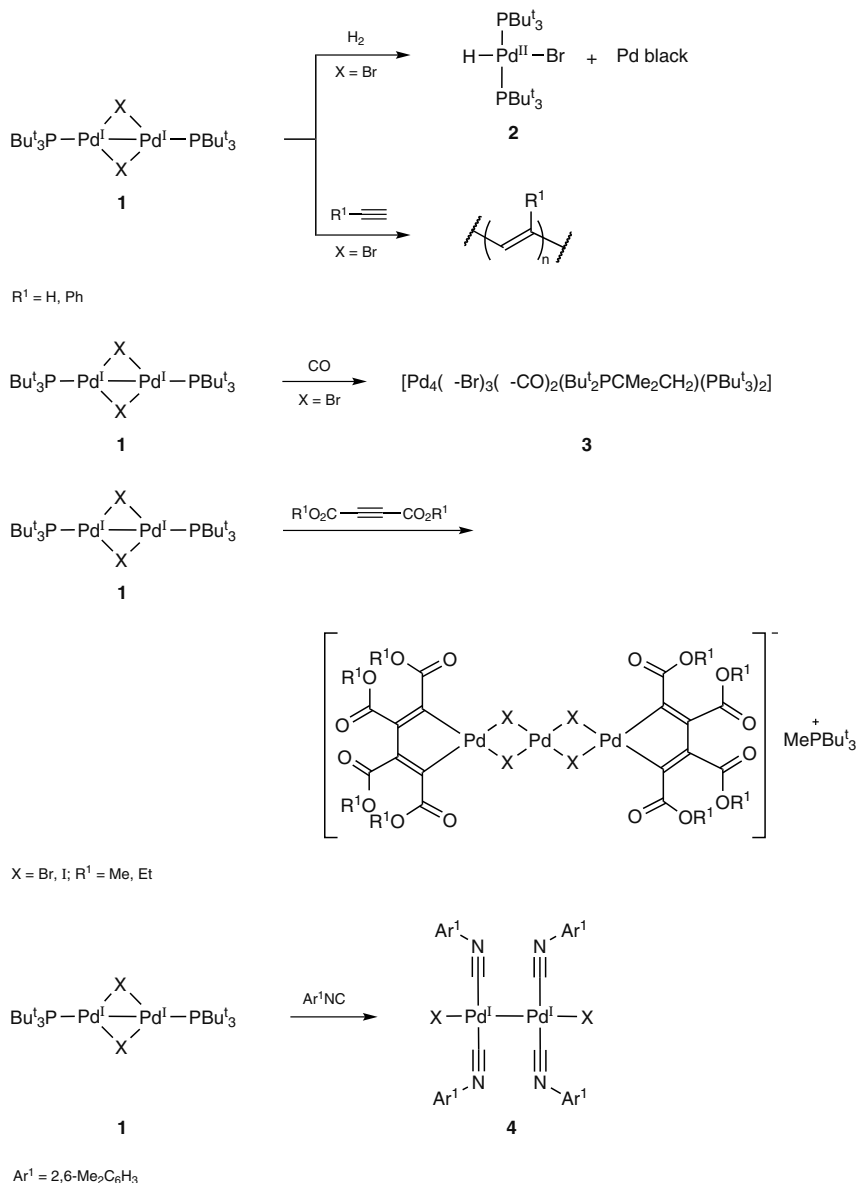
During the evolution of organic chemistry, palladium catalysts have played an important and irreplaceable role in studies on carbon–carbon<sup>[1–7]</sup> and carbon–heteroatom<sup>[8–10]</sup> bond formation. Beyond the methodological studies, palladium-catalyzed reactions have also been widely applied in the preparation of natural products,<sup>[11]</sup> pharmaceuticals, agrochemicals, and materials, even on large scale.<sup>[12]</sup> Palladium(0) and palladium(II) species are frequently used as the catalysts and considered as active intermediates, participating in oxidative addition and reductive elimination steps in two-electron-transfer processes.<sup>[1–15]</sup> Throughout the development of palladium chemistry, an increasing number of single-electron-transfer procedures have been proposed and carefully studied, which mainly involve palladium(I)<sup>[16]</sup> and palladium(III)<sup>[17]</sup> species. The focus of this chapter is on radical-based palladium-catalyzed bond constructions in organic synthesis.

#### 1.2.7.1 Method 1: Reactions Involving Palladium(I) Species

##### 1.2.7.1.1 Variation 1: Synthesis of Organometallic Palladium(I) Complexes

Various palladium(I) complexes have been successfully synthesized, most of which exist as dimers. In previously reported reactions starting from palladium(I) complexes, the palladium species tended to undergo a single-electron oxidation to generate the corresponding palladium(II) complexes in monomeric or dimeric form. Besides the common ligand-exchange reactions, palladium(I) complexes have been transformed with hydrogen, carbon monoxide,<sup>[18,19]</sup> oxygen,<sup>[20]</sup> and even ammonia gas,<sup>[21]</sup> which has helped to further the understanding of palladium chemistry.

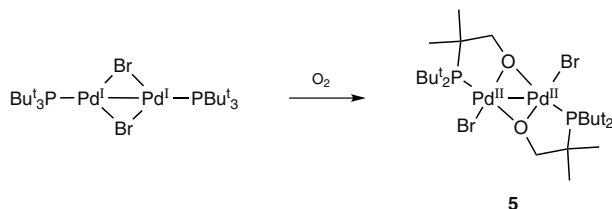
The complexes **1** ( $\{PdX[P(t-Bu)_3]\}_2$ ; X = Br, I) are palladium(I) dimers of great significance that have been successfully isolated and transformed (Scheme 1).<sup>[18,19]</sup> When the dimer **1** (X = Br) is stirred under a hydrogen or carbon monoxide atmosphere, the new palladium hydride species **2** and CO-bridged palladium complex **3**, respectively, can be isolated and characterized. In addition, dimer **1** (X = Br) also reacts with terminal alkynes to produce polyethylene derivatives. When dimer **1** (X = I) is reacted with 1,2-disubstituted alkynes (diethyl or dimethyl but-2-ynedioate), a new trinuclear palladium species is formed.<sup>[19]</sup> Furthermore, an isonitrile also reacts efficiently with dimers **1** to generate new palladium(I) dimers **4**, which have four isonitrile units coordinated.

**Scheme 1** Typical Reactions of Palladium(I) Dimers<sup>[18,19]</sup>

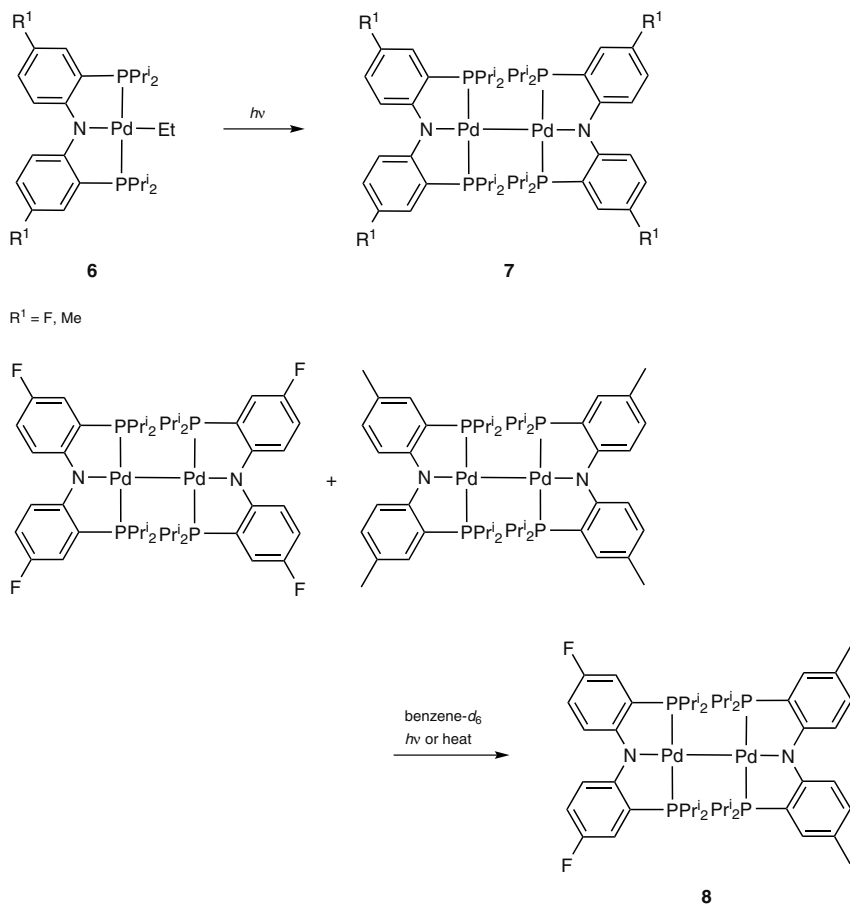
X	Yield (%)	Ref
Br	74	[19]
I	58	[19]

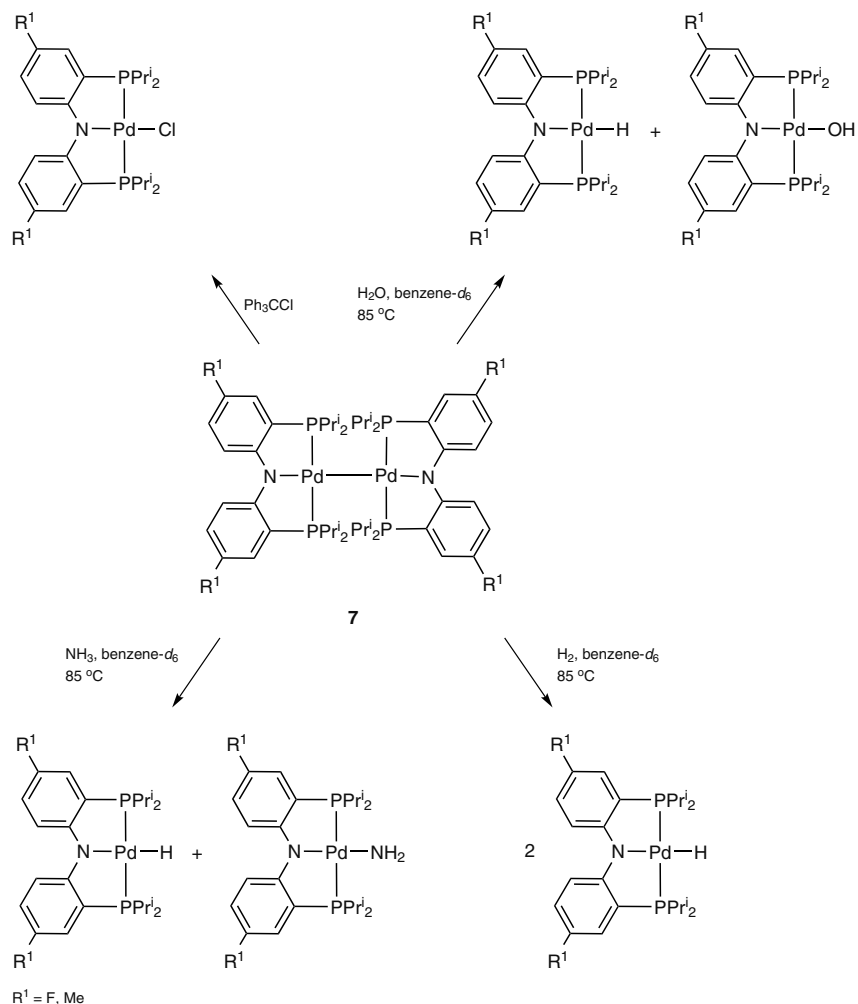
The palladium(I) dimer **1** ( $X = \text{Br}$ ) can be reacted with aerial oxygen to produce the Pd–O–Pd bridge complex **5** through dual intramolecular C–H activation (Scheme 2).<sup>[20]</sup> It has been proposed, but not yet clearly confirmed, that the mechanism might include three steps: (1) coordination between the palladium(I) dimer and molecular oxygen with cleavage of the O=O bond; (2) intramolecular activation of two C–H bonds; and (3) the formation of new C–O bonds. In addition, it is not yet clear whether the two oxygen atoms originate from the same molecule of oxygen.

**Scheme 2** Reaction of a Palladium(I) Dimer with Oxygen<sup>[20]</sup>

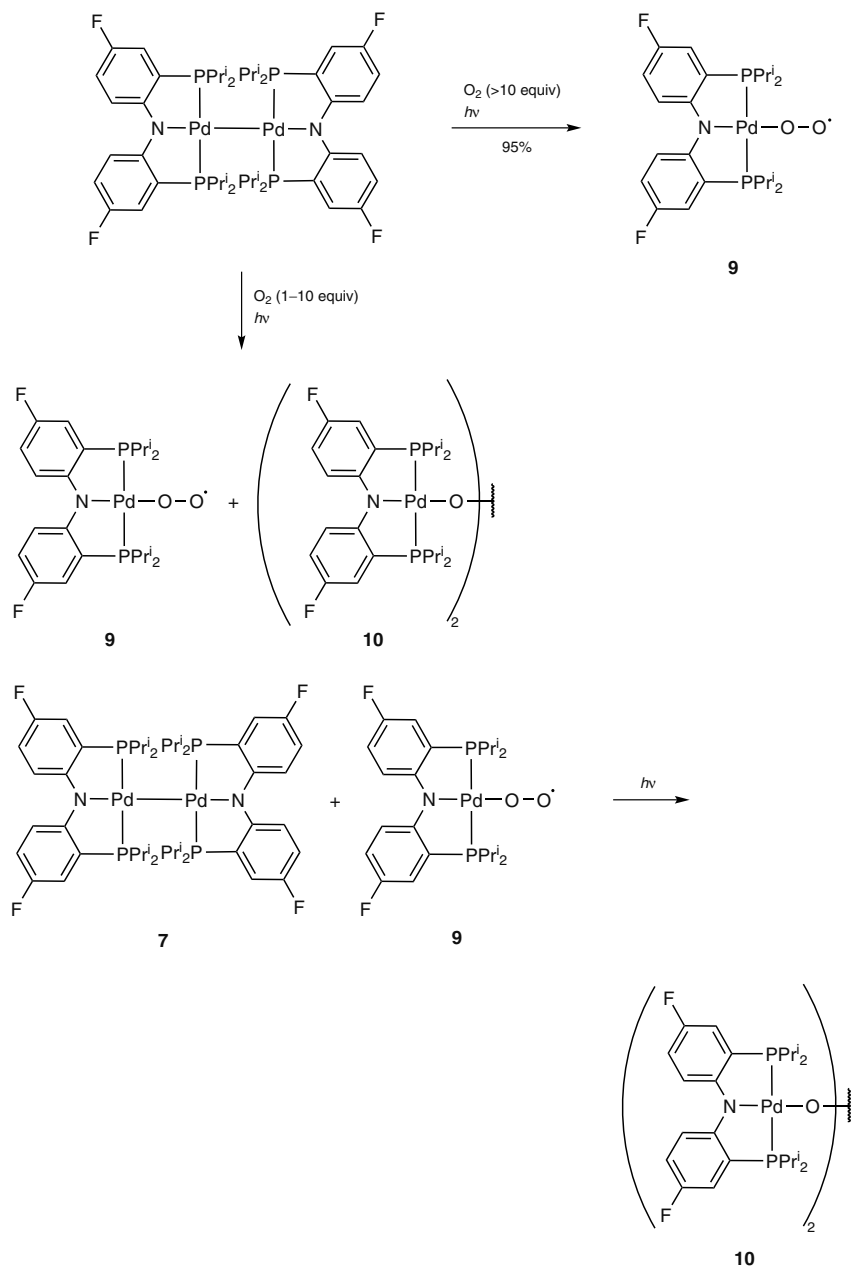


The photochemical homolysis of Pd–C bonds has been observed with the PNP-ligated palladium–alkyl complexes **6**, which form the (PNP)Pd–Pd(PNP) dimers **7** with a single Pd–Pd bond (Scheme 3).<sup>[21]</sup> X-ray diffraction reveals that each palladium center is four-coordinate with a distorted square-planar environment. In addition, electron paramagnetic resonance (EPR) experiments have helped to reveal that the PNP–palladium monomer is reversibly produced in solvent. In fact, thermolysis or photolysis of a 1:1 mixture of **7** ( $R^1 = \text{F}$ ) and **7** ( $R^1 = \text{Me}$ ) in benzene- $d_6$  results in the formation of a ca. 1:1:2 mixture of complexes **7** ( $R^1 = \text{F}$ ), **7** ( $R^1 = \text{Me}$ ), and **8**. More importantly, the palladium(I) dimers **7** react efficiently with dihydrogen, water, or ammonia via binuclear oxidative addition (Scheme 4).<sup>[21]</sup> The reaction with ammonia represents a new mode of activation.

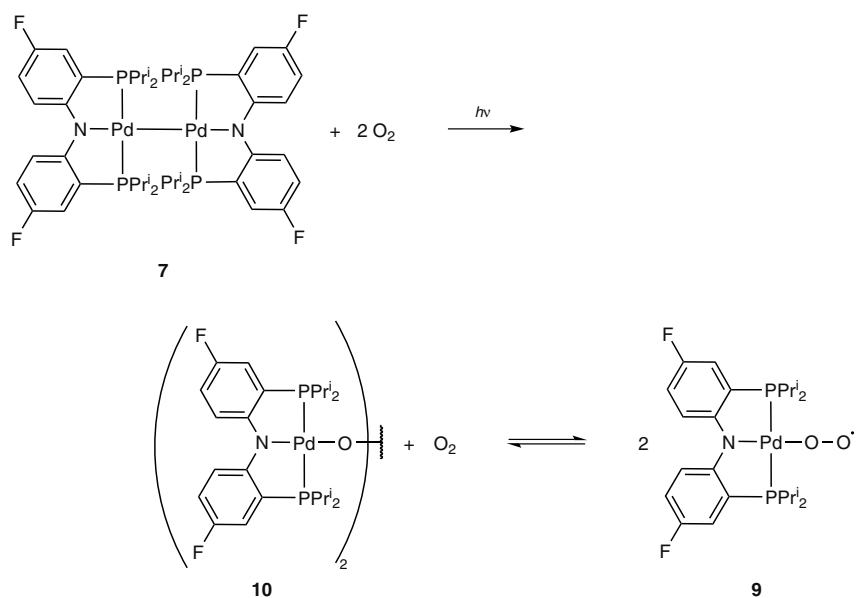
**Scheme 3** Synthesis of (PNP)Pd–Pd(PNP) Dimers<sup>[21]</sup>

**Scheme 4** Oxidative Addition to Palladium(I) Dimers<sup>[21]</sup>

When the palladium(I) dimer **7** ( $R^1 = F$ ) reacts with oxygen (1 atm, >10 equivalents) under irradiation by sunlight, it affords the palladium superoxide complex **9** in 95% yield within 1 minute (Scheme 5).<sup>[22]</sup> The mixture undergoes a rapid color change from the green of complex **7** ( $R^1 = F$ ) to the orange of complex **9**. When the oxygen amount is less than 10 equivalents, the formation of complex **10** can be observed. By combining complex **7** ( $R^1 = F$ ) and **9** in a ca. 1:2 ratio, it is possible to generate the complex **10** in relatively pure form. When the solution of complex **9** was concentrated, and the residue was redissolved and then irradiated, complex **10** was again detected, which further confirms the equilibrium between complexes **9** and **10**. In summary, the reaction between oxygen and dimer **7** ( $R^1 = F$ ) is irreversible, but an equilibrium exists between oxygen, complex **9**, and complex **10** (Scheme 5).

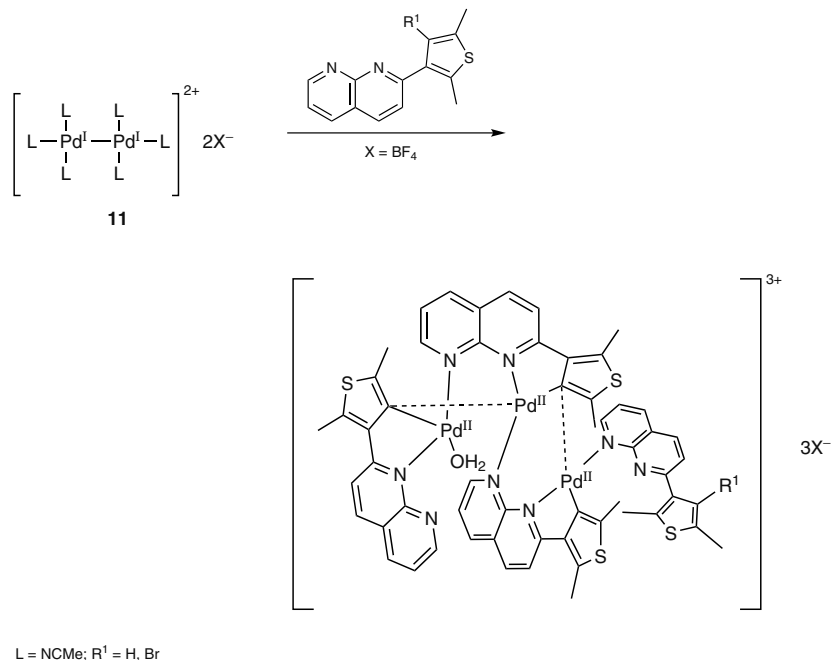
**Scheme 5** Oxidation of a Palladium(I) Dimer with Oxygen<sup>[22]</sup>

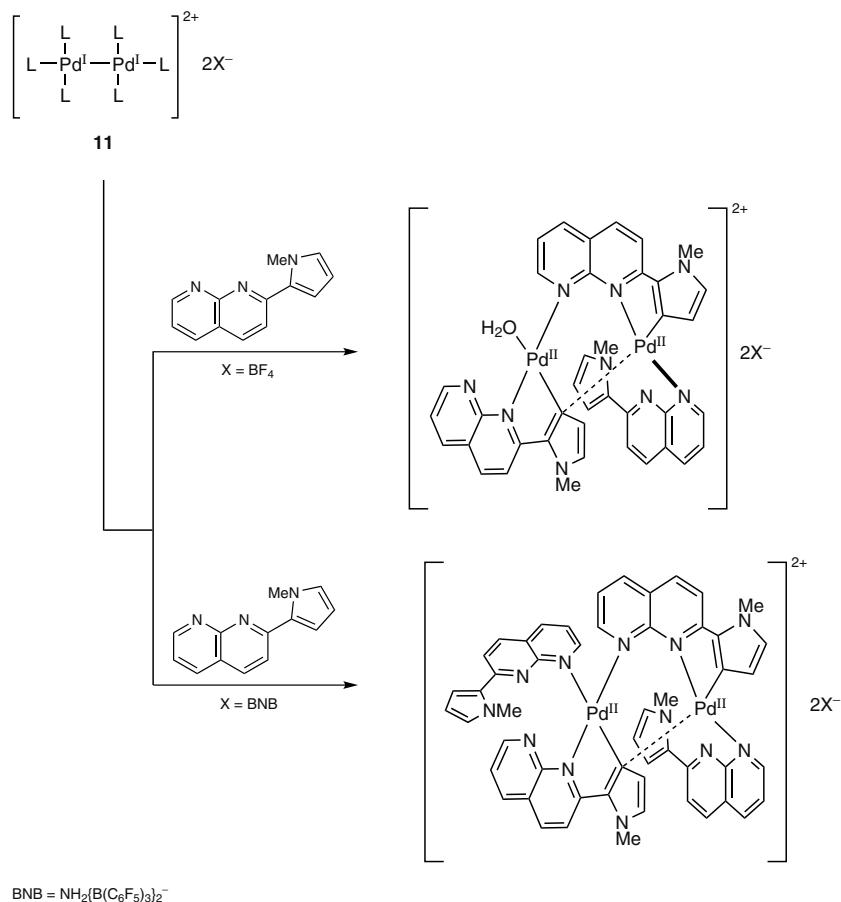




When the solvated complexes  $[\text{Pd}_2(\text{NCMe})_6]\text{X}_2$  **11** [ $\text{X} = \text{BF}_4, \text{NH}_2\{\text{B}(\text{C}_6\text{F}_5)_3\}_2$ ] react with 2-substituted 1,8-naphthyridines, various di- or trinuclear palladium(II) cyclometalated complexes are obtained through C–H/Br activation under mild conditions (Scheme 6).<sup>[23]</sup>

**Scheme 6** Formation of C–H Activated Complexes<sup>[23]</sup>



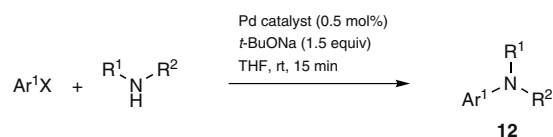


## 1.2.7.1.2

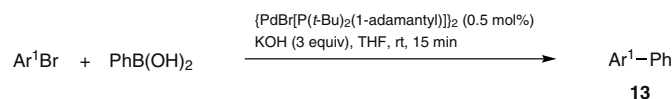
### Variation 2: Reactions Involving Palladium(I) Precatalysts

Most commonly, palladium complexes have been introduced into reaction systems as palladium(0) or palladium(II) species. Since the investigation of palladium(I) catalysts, it has been shown that palladium(I) generally exhibits more efficiency in C–C and C–N bond-forming transformations, which is attributed to the easy generation of active palladium(0) species from the palladium(I) dimer complexes.<sup>[24–27]</sup> Suzuki couplings, Buchwald–Hartwig aminations, carbonylation couplings, and  $\alpha$ -arylation of carbonyl compounds can all be achieved using palladium(I) precatalysts under mild conditions (room temperature) in shortened time (minutes). However, the development of other common cross coupling, oxidative coupling, reductive coupling, and C–H activation reactions is still to be achieved.

The seminal report of a reaction involving a palladium(I) precatalyst is that from Hartwig's group in 2002.<sup>[24]</sup> Air-stable palladium(I) dimers have been utilized to catalyze the coupling between various aryl bromides/chlorides and amines to give arylamines **12** (Scheme 7). The reactions are complete within minutes at room temperature, with excellent yields. The aryl halides can have an electron-withdrawing or electron-donating substituent; *ortho*-substitution is also tolerated. The amines can be secondary aliphatic ones, or primary or secondary aryl ones. Furthermore, the coupling between aryl bromides and phenylboronic acid has been presented, resulting in biaryls **13** (Scheme 8).

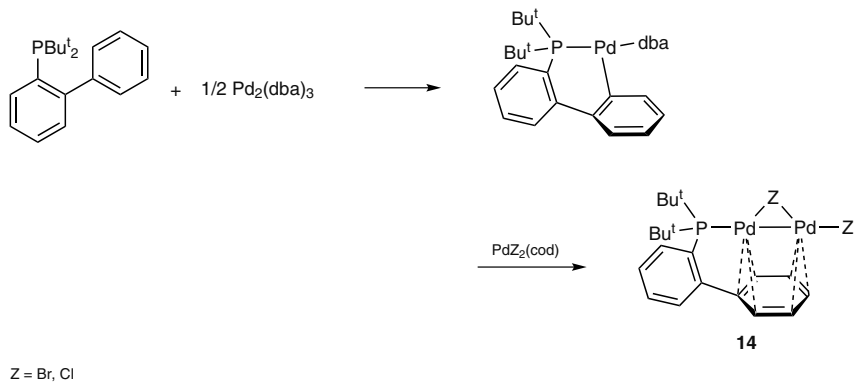
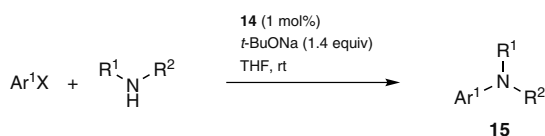
**Scheme 7** Cross Coupling between Aryl Halides and Amines Using Palladium(I) Dimer Catalysts<sup>[24]</sup>

Ar <sup>1</sup>	X	R <sup>1</sup>	R <sup>2</sup>	Catalyst	Yield (%)	Ref
4-Tol	Cl	(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub>		{PdBr[P( <i>t</i> -Bu) <sub>2</sub> (1-adamantyl)] <sub>2</sub> }	92	[24]
4-NCC <sub>6</sub> H <sub>4</sub>	Cl	Bu	Bu	{PdBr[P( <i>t</i> -Bu) <sub>2</sub> (1-adamantyl)] <sub>2</sub> }	93	[24]
4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	Cl	Bu	Bu	{PdBr[P( <i>t</i> -Bu) <sub>3</sub> ] <sub>2</sub> }	97	[24]
4- <i>t</i> -BuO <sub>2</sub> CC <sub>6</sub> H <sub>4</sub>	Cl	Bu	Bu	{PdBr[P( <i>t</i> -Bu) <sub>3</sub> ] <sub>2</sub> }	>99	[24]
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	Br	Bu	Bu	{PdBr[P( <i>t</i> -Bu) <sub>3</sub> ] <sub>2</sub> }	96	[24]
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	Br	Me	Ph	{PdBr[P( <i>t</i> -Bu) <sub>2</sub> (1-adamantyl)] <sub>2</sub> }	98	[24]
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	Br	Ph	Ph	{PdBr[P( <i>t</i> -Bu) <sub>3</sub> ] <sub>2</sub> }	96	[24]

**Scheme 8** Suzuki Coupling Catalyzed by a Palladium(I) Dimer<sup>[24]</sup>

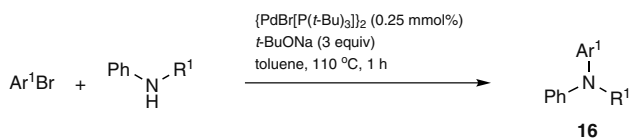
Ar <sup>1</sup>	Yield (%)	Ref
4-Tol	95	[24]
2-NCC <sub>6</sub> H <sub>4</sub>	92	[24]
2-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	90	[24]
2-MeOC <sub>6</sub> H <sub>4</sub>	96	[24]

In 2004, new palladium(I)–palladium(I) dinuclear complexes **14** with one bridging halide were synthesized, in which only one phosphine is retained in the dinuclear core.<sup>[25]</sup> An unprecedented  $\mu^2\text{-}\eta^3\text{:}\eta^3$  coordination mode between a phenyl ring of the biphenyl-2-yl-di-*tert*-butylphosphine ligand and the palladium(I) unit was present in the complexes (Scheme 9). Furthermore, the catalytic ability in the amination of aryl halides was concisely investigated (Scheme 10); both complexes efficiently catalyze the coupling between an aryl bromide/chloride and primary or secondary arylamines to give diarylamines **15**.

**Scheme 9** Synthesis of a Palladium(I)–Palladium(I) Dinuclear Complex<sup>[25]</sup>**Scheme 10** Application of a Palladium(I)–Palladium(I) Dinuclear Complex in Cross Coupling between Aryl Halides and Amines<sup>[25]</sup>

Ar <sup>1</sup>	X	R <sup>1</sup>	R <sup>2</sup>	Catalyst	Time (h)	Yield (%)	Ref
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	Br	Ph	Ph	<b>14</b> (Z = Br)	19	86	[25]
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	Br	Ph	Ph	<b>14</b> (Z = Cl)	19	76	[25]
4-Tol	Cl	4-Tol	H	<b>14</b> (Z = Br)	3	78	[25]
4-Tol	Cl	4-Tol	H	<b>14</b> (Z = Cl)	3	81	[25]

The palladium(I)-catalyzed amination of aryl bromides has been investigated with a focus on the use of secondary alkyl(aryl)amines and aryl bromides bearing electron-donating and electron-withdrawing groups (Scheme 11).<sup>[26]</sup> The reactions using the palladium(I) dimer were conducted in parallel with the use of palladium(II) acetate/tri-*tert*-butylphosphine; generally, the reactions with the palladium(I) dimer as catalyst afford better yields of amines **16**.

**Scheme 11** Cross Coupling between Aryl Halides and Aryl(alkyl)amines<sup>[26]</sup>

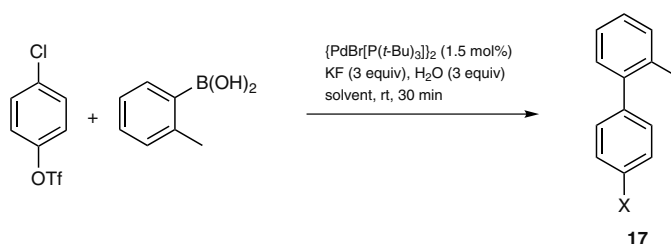
Ar <sup>1</sup>	R <sup>1</sup>	Yield <sup>a</sup> (%)	Ref
Ph	Cy	93 (86)	[26]
3-MeOC <sub>6</sub> H <sub>4</sub>	Cy	94 (89)	[26]
4-FC <sub>6</sub> H <sub>4</sub>	Cy	77 (71)	[26]

Ar <sup>1</sup>	R <sup>1</sup>	Yield <sup>a</sup> (%)	Ref
2-Tol	Cy	60 (52)	[26]
Ph	<i>t</i> -Bu	92 (87)	[26]
3-MeOC <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu	91 (90)	[26]
4-FC <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu	87 (87)	[26]
2-Tol	<i>t</i> -Bu	61 (12)	[26]

<sup>a</sup> Yields using Pd(OAc<sub>2</sub>) (1 mol%) and *t*-Bu<sub>3</sub>P (1 mol%) are given in parentheses.

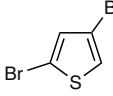
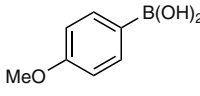
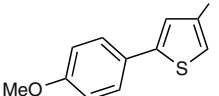
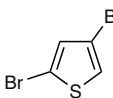
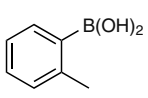
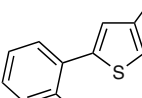
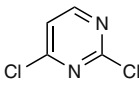
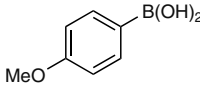
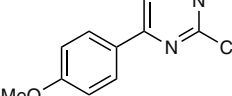
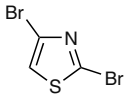
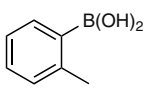
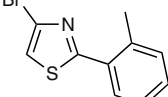
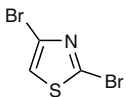
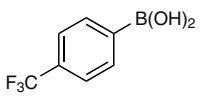
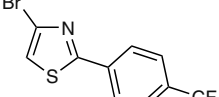
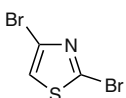
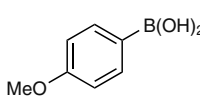
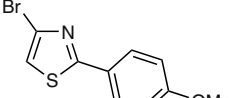
Control of the chemoselectivity of a palladium(I)-catalyzed Suzuki coupling has been realized by adjusting solvent polarity (Scheme 12).<sup>[27]</sup> Thus, reaction of 4-chlorophenyl trifluoromethanesulfonate in a polar solvent (acetonitrile) produces the C–OTf insertion product **17** (X = Cl) selectively; in contrast, use of the less-polar solvent tetrahydrofuran provides the C–Cl insertion product **17** (X = OTf). In addition, regioselective coupling has also been achieved with hetaryl halides **18** (Table 1). In mechanistic studies, <sup>31</sup>P NMR analysis and DFT calculations have been used to show that a Pd(I)L monomer is the real catalyst, and not the dimer. Detailed computational studies suggest that the active catalyst is generated through a reduction instead of homocleavage or direct disproportionation of the precatalyst. Meanwhile, <sup>31</sup>P NMR spectroscopy has confirmed that the combination of an arylboronic acid, potassium fluoride, and water triggers the generation of bis(*tert*-butylphosphine)palladium(0) (Scheme 13). At the same time, a black precipitate forms, which is most likely palladium black. This phenomenon is assigned to the deactivation of catalyst and the incomplete conversion of aryl chlorides in palladium(I)-dimer-catalyzed Suzuki couplings.

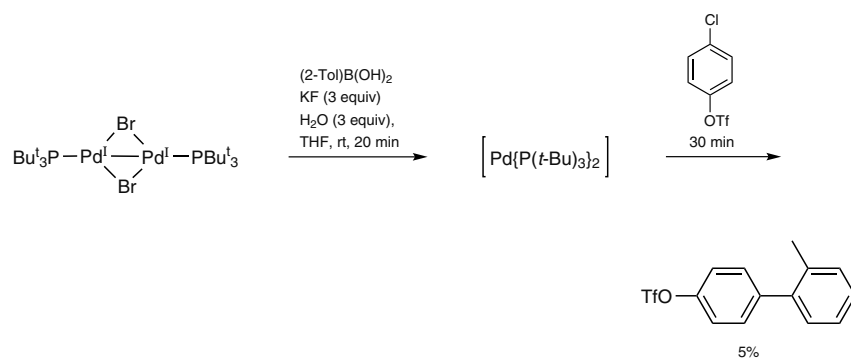
**Scheme 12** Suzuki Coupling of 4-Chlorophenyl Trifluoromethanesulfonate Using a Palladium(I) Catalyst in Different Solvents<sup>[27]</sup>



Solvent	X	Yield (%)	Ref
THF	OTf	76	[27]
MeCN	Cl	78	[27]

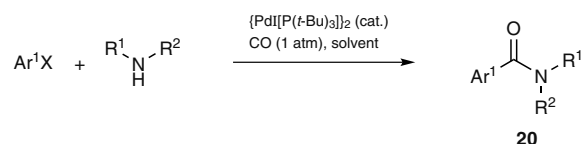
**Table 1** Selective Couplings of Dihalogenated Heterocycles<sup>[27]</sup>

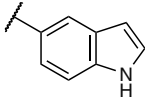
Starting Materials		Product	Yield (%)	Ref
Hetarene	Boronic Acid			
			90	[27]
			92	[27]
			82	[27]
			91	[27]
			87	[27]
			94	[27]

**Scheme 13** Reactivity of 4-Chlorophenyl Trifluoromethanesulfonate with Bis(tri-*tert*-butylphosphine)palladium(0)<sup>[27]</sup>

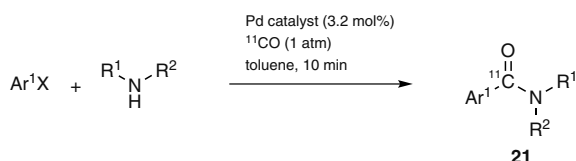
The palladium(I)-catalyzed carbonylative coupling of aryl halides and amines has been achieved under an atmospheric pressure of carbon monoxide (Scheme 14).<sup>[28]</sup> The reactions yield the desired products **20** in moderate to good yields within 10 minutes. Aryl iodides are better substrates than aryl bromides, and can be transformed with a lower catalyst loading and at a lower temperature. In light of the high efficiency, this system has been successfully applied in synthesizing radiolabeled amides **21** using <sup>11</sup>C O gas (Scheme 15).

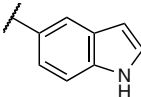
**Scheme 14** Palladium(I)-Catalyzed Carbonylative Coupling of Aryl Halides and Amines<sup>[28]</sup>



Ar <sup>1</sup>	X	R <sup>1</sup>	R <sup>2</sup>	Solvent	Catalyst (%)	Temp (°C)	Yield (%)	Ref
Ph	Br	H	Bn	mesitylene	10	150	46	[28]
4-MeOC <sub>6</sub> H <sub>4</sub>	Br	H	Bn	mesitylene	10	150	46	[28]
2-MeOC <sub>6</sub> H <sub>4</sub>	Br	H	Bn	mesitylene	10	150	46	[28]
	I	(CH <sub>2</sub> ) <sub>5</sub>		toluene	2.2	100	82	[28]

**Scheme 15** Palladium(I)-Catalyzed Carbonylative Coupling of Aryl Halides and Amines Using <sup>11</sup>C O<sub>2</sub><sup>[28]</sup>



Ar <sup>1</sup>	X	R <sup>1</sup>	R <sup>2</sup>	Catalyst	Trapped Radioactivity (%)	<sup>11</sup> C Amide RCP <sup>a</sup> (%)	<sup>11</sup> C Amide RCY <sup>b</sup> (%)	Ref
Ph	Br	H	Bn	{Pd[P( <i>t</i> -Bu) <sub>3</sub> ]} <sub>2</sub>	87	81	70	[28]
Ph	Br	H	Bn	{Pd[P( <i>t</i> -Bu) <sub>3</sub> ]} <sub>2</sub>	72	68	47	[28]
	I	(CH <sub>2</sub> ) <sub>5</sub>		{Pd[P( <i>t</i> -Bu) <sub>3</sub> ]} <sub>2</sub>	78	88	69	[28]

<sup>a</sup> RCP = radiochemical purity.

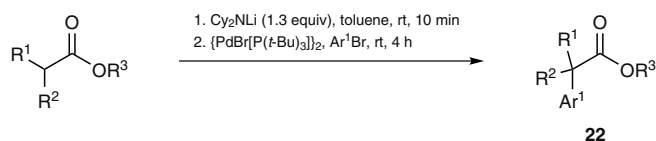
<sup>b</sup> RCY = radiochemical yield.

The cross coupling between aryl bromides and esters can also be catalyzed by {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub> in a process promoted by lithium dicyclohexylamide (Scheme 16).<sup>[29]</sup> The catalyst loading is 0.05–0.5 mol%. The aryl bromides can be substituted by electron-withdrawing or electron-donating groups. In addition, pyridyl and thienyl bromides are also compatible. However, the choice of esters is limited to *tert*-butyl propanoate, methyl

for references see p 111

2-methylpropanoate, and *tert*-butyl acetate. It is worth noting that reactions with all three esters can be conducted on a 10-gram scale.

**Scheme 16**  $\alpha$ -Arylation of Esters Catalyzed by Palladium(I)<sup>[29]</sup>



R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Ar <sup>1</sup>	[PdBr[P( <i>t</i> -Bu) <sub>3</sub> ] <sub>2</sub> ] (mol%)	Yield (%)	Ref
H	H	<i>t</i> -Bu	4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	0.20	83	[29]
H	H	<i>t</i> -Bu	4-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	0.40	73	[29]
H	H	<i>t</i> -Bu	4-FC <sub>6</sub> H <sub>4</sub>	0.40	82	[29]
Me	H	<i>t</i> -Bu	4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	0.04	87 <sup>a</sup>	[29]
Me	H	<i>t</i> -Bu	4-FC <sub>6</sub> H <sub>4</sub>	0.20	88	[29]
Me	H	<i>t</i> -Bu	2,4,6-Me <sub>3</sub> C <sub>6</sub> H <sub>2</sub>	0.05	72	[29]
Me	Me	Me	4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub>	0.05	72	[29]
Me	Me	Me	4-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	0.50	60	[29]
Me	Me	Me	2-pyridyl	0.50	71	[29]
Me	Me	Me	3-thienyl	0.50	75	[29]

<sup>a</sup> Reaction was performed on a 40-mmol scale.

### Arylamines 12; General Procedure:<sup>[24]</sup>

In a drybox, the Pd catalyst (0.005 M in THF), *t*-BuONa (144.0 mg, 1.50 mmol), an aryl halide (1.00 mmol), and an amine [1.05 mmol in THF (1 mL)] were added to a vial containing a stirrer bar. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The mixture was then stirred at rt for 15 min. After this time, H<sub>2</sub>O (1 mL) was added into the vial, and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was dried (MgSO<sub>4</sub>) and concentrated, and the residue was purified by column chromatography.

### Biaryls 13; General Procedure:<sup>[24]</sup>

In a drybox, {PdBr[P(*t*-Bu)<sub>3</sub>]<sub>2</sub>} (0.005 M in THF), KOH (168.0 mg, 3.0 mmol), PhB(OH)<sub>2</sub> (1.08 mmol), and an aryl bromide [1.00 mmol in THF (1.5 mL)] were added to a vial containing a stirrer bar. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The mixture was then stirred at rt for 15 min. After this time, H<sub>2</sub>O (1 mL) was added into the vial, and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was dried (MgSO<sub>4</sub>) and concentrated, and the residue was purified by column chromatography.

### Arylamines 15; General Procedure:<sup>[25]</sup>

To an argon-filled Schlenk tube containing a mixture of the catalyst **14** (0.01 mmol), *t*-BuONa (1.4 mmol), an aryl halide (1.0 mmol), and an amine (1.2 mmol) was added THF (1 mL). The resulting mixture was stirred at rt until the aryl halide was consumed, and then it was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was dried (MgSO<sub>4</sub>) and concentrated, and the residue was purified by column chromatography (silica gel, hexane/EtOAc).



**Alkyldiarylamines 16; General Procedure:**<sup>[26]</sup>

To an argon-flushed, three-necked flask, containing Pd(OAc)<sub>2</sub> (12.8 mg, 0.057 mmol) or {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub> (22.0 mg, 0.0285 mmol), *t*-BuONa (1.64 g, 17.1 mmol), an aniline (5.7 mmol), and an aryl bromide (6.9 mmol), was added dry, degassed toluene (20 mL). After stirring at rt for 15 min, *t*-Bu<sub>3</sub>P [only in the cases where Pd(OAc)<sub>2</sub> was used; 11.5 mg, 0.057 mmol] dissolved in toluene was added. Then, the mixture was heated to 108–110 °C and kept at the same temperature for 1 h. After cooling to rt, the reaction was quenched with H<sub>2</sub>O (10 mL), and then the organic layer was washed with H<sub>2</sub>O and concentrated. The crude product was purified by chromatography (silica gel).

**2'-Methyl-[1,1'-biphenyl]-4-yl Trifluoromethanesulfonate (17, X = OTf) or 4'-Chloro-2-methyl-1,1'-biphenyl (17, X = Cl); General Procedure:**<sup>[27]</sup>

A N<sub>2</sub>-filled dry reaction vessel was charged with 4-chlorophenyl trifluoromethanesulfonate (276.0 mg, 1.1 mmol), 2-tolylboronic acid (146 mg, 1.1 mmol), and KF (186 mg, 3.2 mmol). After the vessel was transferred to a drybox, THF or MeCN (2 mL; previously deoxygenated for 30 min) and H<sub>2</sub>O (3.0 equiv) were added and the mixture was stirred for 5 min. Then, {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub> (12.4 mg, 0.016 mmol) was added and the mixture was stirred at rt for 30 min. The resulting mixture was subsequently diluted with Et<sub>2</sub>O and filtered through silica using Et<sub>2</sub>O as the eluant. The filtrate was concentrated in vacuo and purified by column chromatography.

**Hetarenes 19; General Procedure:**<sup>[27]</sup>

In a glovebox, to a N<sub>2</sub>-filled dry reaction vessel containing the heterocyclic substrate (0.5 mmol) was added recrystallized, deoxygenated, and dried boronic acid (0.5 mmol), KF (87.0 mg, 1.5 mmol), and deoxygenated THF (1 mL). The mixture was stirred for 5 min and then {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub> (4.1 mg, 0.005 mmol), THF (0.5 mL), and H<sub>2</sub>O (3.0 equiv) were added (THF and H<sub>2</sub>O were deoxygenated prior to use). After this, the mixture was stirred for an additional 30 min. Then, the mixture was quenched with Et<sub>2</sub>O and filtered through silica gel, the filtrate was concentrated, and the residue was purified by column chromatography.

**Benzamides 20; General Procedure:**<sup>[28]</sup>

**CAUTION:** Carbon monoxide is extremely flammable and toxic, and exposure to higher concentrations can quickly lead to a coma.

To a CO-filled Schlenk tube, containing the catalyst complex (2.2 or 10 mol%), was added the aryl halide (0.45 mmol) and the amine (BnNH<sub>2</sub> or piperidine; 4.6 mmol) in the stated solvent. The mixture was stirred in a preheated oil bath for the desired time. Then, the reaction was quenched with 1 M aq HCl (4.5 mL). The rubber septum was removed and the unreacted CO was vented into the fumehood. The crude product mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 5 mL), the extracts were filtered and concentrated, and the residue was purified by column chromatography (silica gel).

For the preparation of <sup>11</sup>C-radiolabeled benzamides, the procedure was as described above but with the use of <sup>11</sup>CO instead of CO.

**α-Aryl Esters 22; General Procedure with *tert*-Butyl Propanoate:**<sup>[29]</sup>

In a drybox, to a 4-mL, screw-capped vial containing Cy<sub>2</sub>NLi (0.243 g, 1.30 mmol) dissolved in toluene (2 mL), was slowly added the ester (1.10 mmol). After stirring at rt for 10 min, the soln was added to another 4-mL, screw-capped vial containing the aryl bromide (1.00 mmol) and catalyst {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub>. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. After stirring at rt for 4 h, the mixture was diluted with Et<sub>2</sub>O (30 mL) and then washed with 0.1 M HCl (10 mL). The aqueous phase was extracted with Et<sub>2</sub>O (3 × 10 mL). To the combined organic layers was added sat. aq NaHCO<sub>3</sub>

(30 mL), and the aqueous layer was back-extracted with Et<sub>2</sub>O (3 × 10 mL). The combined organic layers were washed with H<sub>2</sub>O (30 mL), the aqueous layer was extracted with Et<sub>2</sub>O (3 × 10 mL), and the combined organic layers were dried (MgSO<sub>4</sub>), and concentrated. The crude product was purified by flash column chromatography (silica gel, 2.5% EtOAc in hexanes).

***tert*-Butyl (4-*tert*-Butylphenyl)acetate (22, R<sup>1</sup> = R<sup>2</sup> = H; R<sup>3</sup> = *t*-Bu; Ar<sup>1</sup> = 4-*t*-BuC<sub>6</sub>H<sub>4</sub>); Typical Procedure on a Large Scale:**<sup>[29]</sup>

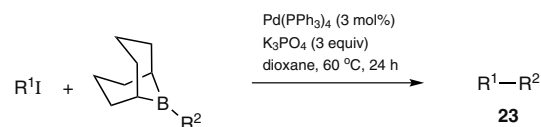
To a N<sub>2</sub>-filled, 500-mL, three-necked round-bottomed flask equipped with a rubber septum, a glass stopper, and a stirrer-bar, was added Cy<sub>2</sub>NH (10.3 mL, 0.052 mol) dissolved in toluene (300 mL). The mixture was stirred for 10 min at 0 °C, and then a 2.5 M soln of BuLi in hexane (20.7 mL, 0.052 mol) was added slowly to the cooled soln. Then, the mixture was stirred for 30 min at 0 °C. *tert*-Butyl acetate (5.93 mL, 0.044 mol) was added slowly over 20 min. The mixture was stirred for an additional 50 min at 0 °C. To another N<sub>2</sub>-filled, pear-shaped, 10-mL flask, containing {PdBr[P(*t*-Bu)<sub>3</sub>]}<sub>2</sub> (0.062 g, 0.0790 mmol), were added 1-bromo-4-*tert*-butylbenzene (6.93 mL, 0.040 mol) and toluene (5 mL). The mixture was transferred via cannula to the round-bottomed flask containing the lithium enolate of *tert*-butyl acetate. Toluene (2 × 5 mL) was used to wash the pear-shaped flask, and the wash was transferred to the round-bottomed flask. The mixture was stirred for 4 h at rt, and then concentrated until the reaction volume was reduced to half by rotary evaporation. A sat. aq soln of NH<sub>4</sub>Cl (300 mL) was added, and the aqueous phase was washed with Et<sub>2</sub>O (5 × 200 mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered, concentrated, and purified; yield: 7.90 g (79.5%).

1.2.7.1.3

**Variation 3:  
Cross-Coupling Reactions**

Palladium-catalyzed cross-coupling reactions have been studied for about half a century. The typical mechanism involves oxidative addition and reductive elimination via two-electron transfer. Cross-coupling reactions involving alkyl halides, especially those with β-hydrogen atoms, are a challenge because of the slow rate of oxidative addition and the rapid rate of β-hydrogen elimination.<sup>[30]</sup> At the same time, cross-coupling reactions of the related alkylmetal compounds are also difficult because of the slow rate of transmetalation.<sup>[31]</sup> Recently, reactions that proceed via single-electron transfer processes have been developed, which have partially solved these problems. Generally, the radical properties of the reaction systems are supported by various radical-trapping experiments.

Cross coupling between 9-alkyl-9-borabicyclo[3.3.1]nonane (9-alkyl-9-BBN) derivatives and alkyl iodides has been achieved in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0) (Scheme 17).<sup>[30]</sup> Primary iodides, even including iodomethane, deliver the products **23** in 45–71% yield; neopentyl iodide (1-iodo-2,2-dimethylpropane) also reacts successfully. However, reactions with secondary iodides are not successful. In terms of the boranes, various functionalized compounds are tolerated, including the presence of alkene, ester, and acetal groups.

**Scheme 17** Cross-Coupling Reactions of 9-Alkyl-9-borabicyclo[3.3.1]nonane Derivatives with Alkyl Iodides<sup>[30]</sup>

R <sup>1</sup>	R <sup>2</sup>	Yield (%)	Ref
Me	(CH <sub>2</sub> ) <sub>10</sub> CO <sub>2</sub> Me	71	[30]
(CH <sub>2</sub> ) <sub>5</sub> Me	(CH <sub>2</sub> ) <sub>7</sub> Me	64	[30]
(CH <sub>2</sub> ) <sub>5</sub> Me		58	[30]
(CH <sub>2</sub> ) <sub>5</sub> Me	(CH <sub>2</sub> ) <sub>10</sub> CO <sub>2</sub> Me	54	[30]
(CH <sub>2</sub> ) <sub>3</sub> CN		61	[30]
(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> Me		57	[30]
(CH <sub>2</sub> ) <sub>9</sub> Me	( <i>E</i> )-CH=CHBu	64	[30]
(CH <sub>2</sub> ) <sub>9</sub> Me	Ph	55	[30]

In 1987, reactions of polyfluoroalkyl iodides with organostannanes in a tetrakis(triphenylphosphine)palladium(0)-catalyzed Negishi coupling were reported (Table 2).<sup>[32]</sup> The stannane can be allyl-, alkenyl-, and alkynyl-substituted. It is worthy to note that even trifluoriodomethane leads to the desired product, albeit with lower yield (entry 3). Both the *E*- and *Z*-isomers of alkenylstannanes react with an iodide to afford only products with *E* configuration (entries 1, 2, 9, and 10). A possible mechanism is the addition of a polyfluoroalkyl radical to the alkenylstannane, followed by the elimination of tributyl-iodostannane; the palladium(0) species is thought to act as a radical initiator (Scheme 18).

**Table 2** Cross Coupling of Polyfluoroalkyl Iodides and Organostannanes<sup>[32]</sup>

Reaction		Catalyst		Solvent		Product		Yield (%)		Ref	
$R^1-CH=CH-SnBu_3 + R^2I$		$Pd(PPh_3)_4$ (10 mol%)		hexane		$R^1-CH=CH-R^2$					
Entry	Starting Materials	Equiv of iodide	Temp	Time (h)	Product	Yield (%)	Ref				
	Stannane	Alkyl iodide									
1		$F_3C(CF_2)_3I$	2	70 °C	4		70	[32]			
2		$F_3C(CF_2)_3I$	2	70 °C	4		70	[32]			
3		$CF_3I$	excess	80 °C	3		11 <sup>a</sup>	[32]			
4		$F_3C(CF_2)_5I$	1.2	rt	1		100	[32]			
5		$F_3C(CF_2)_5I$	3	70 °C	3		64	[32]			
6		$F_3C(CF_2)_3I$	2	70 °C	4		68	[32]			
7		$F_3C(CF_2)_5I$	2	70 °C	6		55	[32]			
8		$F_3C(CF_2)_3I$	2	70 °C	6		60	[32]			
9		$F_3CCH_2I$	2	80 °C	4		38 <sup>a</sup>	[32]			
10		$F_3CCH_2I$	2	80 °C	4		35 <sup>a</sup>	[32]			

<sup>a</sup> Benzene was used as solvent.

**Scheme 18** Possible Mechanism for the Introduction of a Polyfluoroalkyl Group to (*E*)-Tributyl(styryl)stannane<sup>[32]</sup>