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Cobalt-Catalyzed Cross-Coupling Reactions

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1. Introduction

Since the pioneering work of Kharasch[1] on the metal-catalyzed homocoupling reaction of aromatic Grignard reagents (see 2) in the middle of the 20th century, cobalt-catalyzed carbon–carbon bond-forming reactions have received particular attention.[2] The scope of these reactions is different from that of the palladium- and nickel-mediated procedures. Thus, cobalt-catalyzed cross-coupling reactions are very efficient for the elaboration of $C_{sp^2}-C_{sp^2}$ bonds (see section 2), but they are especially interesting for couplings involving alkyl halides, since the decomposition by β-hydrogen elimination of alkyl-cobalt intermediates is not a limitation as in the case of palladium or nickel catalyzed reactions (see sections 3, 4, and 5). Cobalt-mediated acylations, radical cyclizations, and Heck-type reactions have also been described (see sections 6 and 7). All these reactions will be discussed hereafter.

It is worthy of note that cobalt salts have also been extensively used as catalysts for Pauson-Khand[3] and hydroformylation[4] reactions but also for the cyclopropanation[5] of olefins and for $[2+2+2]$[6] and $[2+2]$[7] cycloaddition reactions. These reactions will not be discussed herein.

2. Homocoupling Reactions

The first reports on cobalt-catalyzed cross-coupling reactions describe the homocoupling reaction of Grignard reagents. In 1939, Gilman and Lichtenwalter[8] obtained nearly quantitative yields of homocoupling product by treating aromatic Grignard reagents with a stoichiometric amount of cobalt chloride. In 1941, Kharasch[1] discovered that good yields of homocoupling products are obtained by using only catalytic amounts (i.e., 3 mol %) of cobalt chloride and a stoichiometric amount of an oxidant such as aromatic or aliphatic halides (Scheme 1). The role of this latter is to oxidize the Cobalt(0) species into a cobalt(II) species after the reductive elimination step.

Twenty years later, in 1962, Morizur applied the Kharasch reaction to the synthesis of various biaryls.[9a] The yields are

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Gérard Cahiez received his Ph.D. in 1973, at the University Pierre & Marie Curie (Paris VI), under the supervision of Professor Jean François Normant, on the carbocupration of terminal alkynes (vinyl copper reagents). Then, he joined the CNRS. After a postdoctoral year in the Roussel Uclaf Laboratories (now Sanofi Aventis) on the chemistry of steroid, he came back to the University Pierre and Marie Curie, and in 1980, he became Director of Research at the CNRS. Then, he moved to the *Ecole Supérieure de Chimie Organique et Minérale* (ESCOM, Cergy-Pontoise) in 1993. From 1993 to 2008 he was Director of Research at the CNRS and Professor of Chemistry at ESCOM. From 2000 to 2009, he was also Director of the UMR 8123, a joint research unit CNRS−University of Cergy Pontoise−ESCOM. In 2009, he moved to the University of Paris 13, as Director of Research at the CNRS, to create a new research group in organometallic chemistry. The research developed since 1973 dealt with the use of organometallic reagents in organic synthesis and especially with the development of the chemistry of organomanganese reagents. His current interest is always focused on organomanganese chemistry but more generally on the search for new highly selective organometallic reactions, *i.e.*, Mn-, Co-, and Fe-catalyzed cross-coupling reactions, involving no toxic and expensive metal or additive.

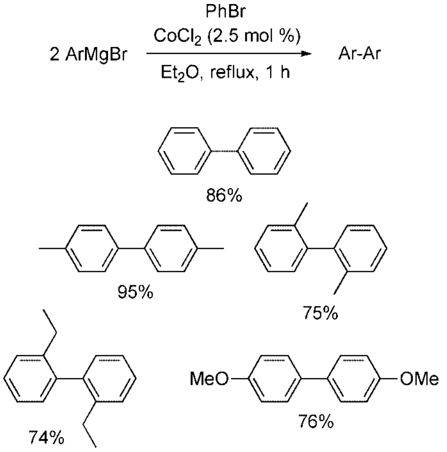
Alban Moyeux was born in La Bassée (France) in 1982. He obtained his B.Sc. Degree from the University of Lens in 2004. He obtained his M.Sc. Degree from the University of Cergy-Pontoise in 2005. He then worked on iron- and cobalt-catalyzed cross-coupling reactions under the supervision of Professor Gérard Cahiez and was awarded his Ph.D. Degree in November 2008. He finally joined the group of Professor Alois Fürstner as a postdoctoral fellow at the Max-Planck Institute of Mülheim (Germany), where he is currently working on total synthesis.

significantly lower than those previously reported by Kharasch. Almost identical results were obtained by using butyl bromide (Scheme 2) or bromobenzene (Table 1) as an oxidant.

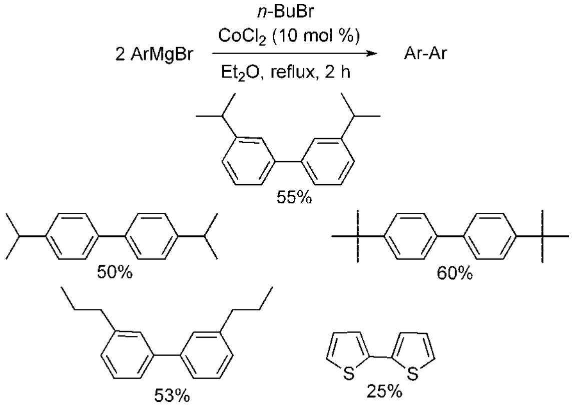
It should be underlined that aryllithium and arylmagnesium compounds give similar yields[9b] (Table 1).

Interestingly, benzylic or homobenzylic Grignard reagents can also be used (Table 1, entries 6−10).

Scheme 1. The Kharasch Reaction



Scheme 2. Cobalt-Catalyzed Homocoupling Reaction of Aromatic Grignard Reagents



3. $C_{sp^2}-C_{sp^2}$ Cross-coupling Reactions

3.1. Alkenylation

3.1.1. From Aromatic Organomagnesium Reagents

In 1943, Kharasch described the first cobalt-catalyzed alkenylation of aromatic Grignard reagents[10] (Table 2).

The very reactive vinyl or 1-propenyl halides give moderate yields (Table 2, entries 1−3) whereas sterically hindered or more substituted alkenyl halides only afford very poor results. Large amounts of homocoupling products are then obtained from both alkenyl halide and aryl Grignard reagent (Table 2, entries 4−6). The synthetic interest of this reaction is limited, since, even in the best cases, 2 equiv of alkenyl halides are used.

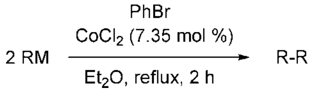
In 1982, Uemura reported the cross-coupling reaction between aryl Grignard reagents and alkenyl tellurides under cobalt catalysis[11] (Scheme 3).

Yields are quantitative, but a large excess of Grignard reagent is used (2.5 equiv). It should be underlined that a substantial amount of homocoupling product (biaryl) is formed as a side product. This is a clear drawback, since the purification of the final product is often tricky.

In 1998, Cahiez reinvestigated the cobalt-catalyzed alkenylation of aromatic Grignard reagents.[12] A clear improvement was observed by using a THF/NMP mixture as a solvent (Table 3). Thus, various alkenyl halides have been coupled stereospecifically in good to excellent yields (Table 3, entries 1−5).

Very recently, Hayashi[13] described the cobalt-catalyzed coupling between alkenyl triflates and aryl Grignard reagents.

Table 1. Cobalt-Catalyzed Homocoupling Reaction of Aryllithium and Arylmagnesium Halides



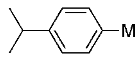
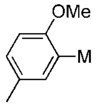
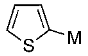
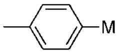
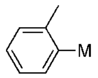
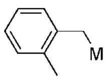
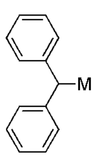
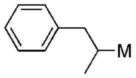
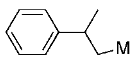
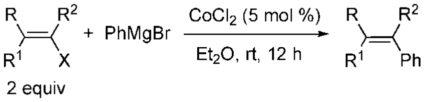
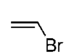
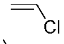
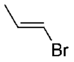
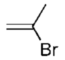
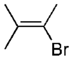
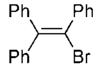
Entry	RM	R-R Yield (%)	
		M = MgBr	M = Li
1		50	60
2		55	65
3		25	30
4		/	60
5		/	65
6		55	60
7		55	60
8		53	/
9		55	/

Table 2. Cobalt-Catalyzed Alkenylation of Aromatic Grignard Reagents



Entry	Alkenyl Halide	Yield (%)
1		56
2		56
3		51
4		23
5		7
6		0

The coupling takes place under mild conditions (Scheme 4). The presence of NMP is not necessary, but PPh_3 is used as a ligand.

This method can be complementary to the precedent method using alkenyl bromides, since vinyl triflates can be easily prepared from the corresponding ketones.

Scheme 3. Cross-coupling between Alkenyl Tellurides and Aromatic Grignard Reagents

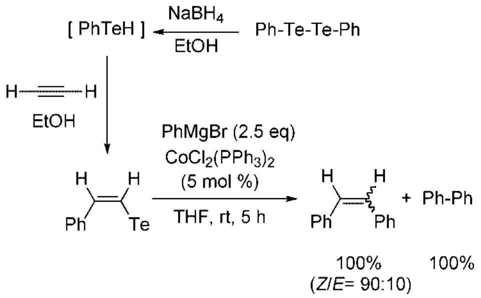
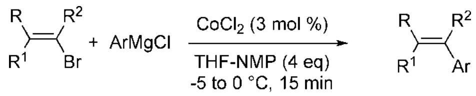
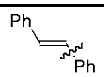
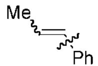
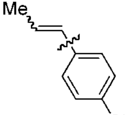
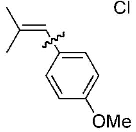
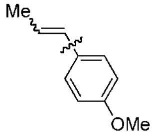
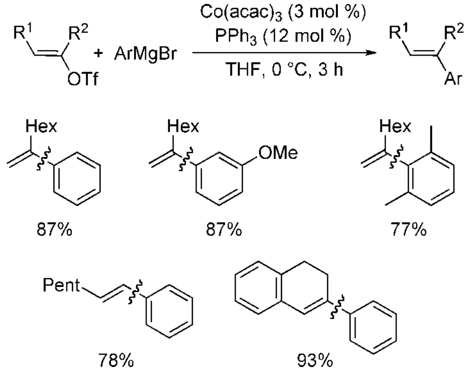


Table 3. Cobalt-Catalyzed Alkenylation of Aromatic Grignard Reagents in the Presence of NMP



Entry	Product	Yield (%)
1		90
2		83
3		55
4		71
5		80

Scheme 4. Cobalt-Catalyzed Cross-coupling between Alkenyl Triflates and Aromatic Grignard Reagents

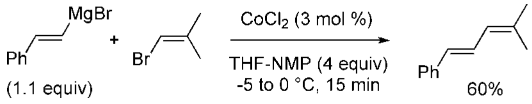


3.1.2. From Vinylic Grignard Reagents

Until now, there have only been very few cobalt-catalyzed alkenyl—alkenyl cross-coupling reactions. In 1998, Cahiez[12] described one example of cobalt-catalyzed cross-coupling between an alkenyl halide and an alkenyl Grignard reagent (Scheme 5) in moderate yield. The reaction is stereospecific and gives only the pure *trans*-diene.

Recently, Hayashi[13] described the cobalt-catalyzed cross-coupling between alkenyl triflates and alkenyl Grignard reagents. Good yields are obtained from α-monosubstituted

Scheme 5. Cobalt-Catalyzed Coupling between Styrylmagnesium Bromide and 2-Methyl-1-bromopropane



Scheme 6. Cobalt-Catalyzed Coupling between Alkenylmagnesium Halides and Alkenyl Triflates

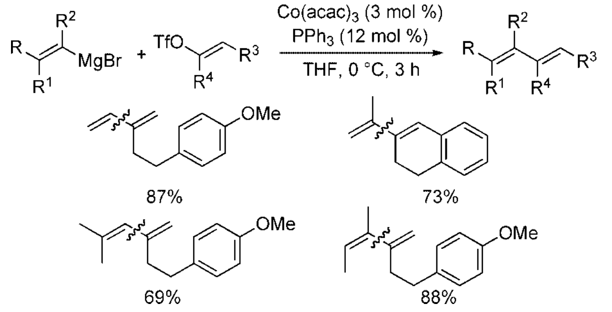
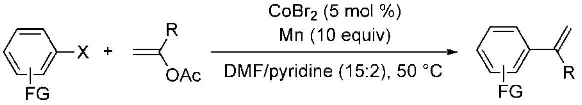
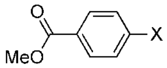
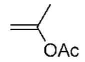
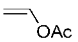
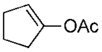
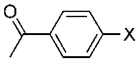
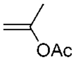
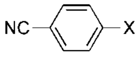
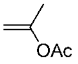
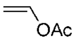
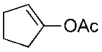
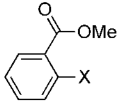
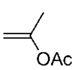
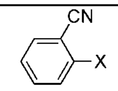
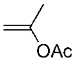


Table 4. Cobalt-Catalyzed Coupling between Functionalized Aryl Halides and Alkenyl Acetates



Entry	Aryl Halide		Alkenyl Acetate	Yield (%)
1		X= Cl		75
2		X= Br		75
3		X= Cl		81
4		X= Cl		79
5		X= Cl		65
6		X= Br		51
7		X= Cl		76
8		X= Br		42
9		X= Cl		37
10		X= Cl		23
11		X= Cl		0
12		X= Br		0
13		X= Cl		73
14		X= Br		16

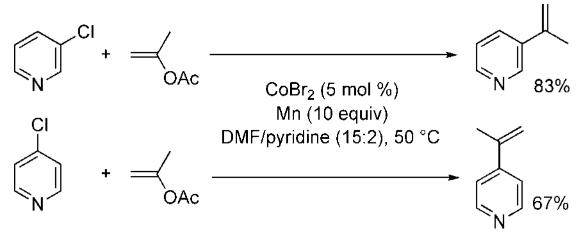
or α,β- and β,β-disubstituted alkenyl Grignard reagents (Scheme 6).

3.1.3. From Aryl Halides and Alkenyl Acetates

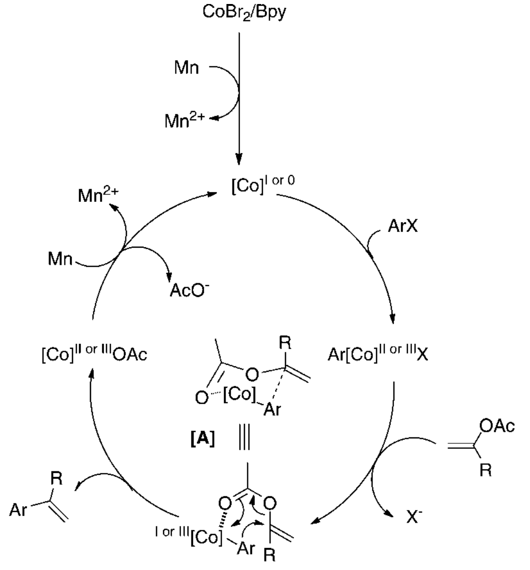
In 2005, Périchon reported the cobalt-catalyzed coupling between functionalized aryl halides and alkenyl acetates. It is the only example of a cobalt-catalyzed arylation of enol esters. The reaction is performed by using a catalytic amount of cobalt bromide (5%) in the presence of 10 equiv of manganese (Table 4).[14]

Moderate to good yields are obtained. As a rule, aryl chlorides or bromides give similar results (Table 4, entries 1−6). However, in some cases, aryl chlorides lead to better yields (2- and 4-halobenzonitriles, entries 7−8 and 13−14).

Scheme 7. Cross-coupling between Chloropyridines and Isopropenyl Acetate



Scheme 8. Mechanism Proposal for the Cobalt-Catalyzed Alkenylation of Aryl Halides by Vinyl Acetates



Aryl iodides such as 4-iodoanisole and ethyl 4-iodobenzoate are not suitable substrates, since they lead essentially to a mixture of reduced and homocoupling products.

The reaction was extended to halopyridines (Scheme 7).

A mechanistic pathway was proposed (Scheme 8). In the first step, Co^{II} is reduced by manganese powder in the presence of pyridine either in Co^{I} or in Co^{0}. In a precedent work, Périchon demonstrated that Co^{I} is stabilized by vinylic acetate in an acetonitrile/pyridine mixture.[15] The low-valent cobalt species formed is probably coordinated by the vinyl acetate. It then undergoes an oxidative addition of the aryl halide to give an "arylcobalt" species. This species could then react with vinylic acetate according to a six-membered transition state [A]. After reductive elimination, cobalt is reduced by the excess of Mn^{0} to regenerate the active cobalt species.

3.2. Aryl−Aryl Cross-coupling

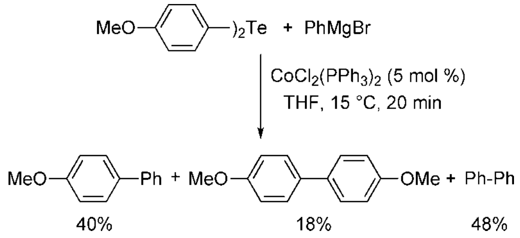
3.2.1. From Aromatic Organometallic Reagents

In 1983, Uemura described the cross-coupling between diaryltellurides (Ar$_2$Te) and aromatic organomagnesium reagents in the presence of cobalt salts[11] (Scheme 9).

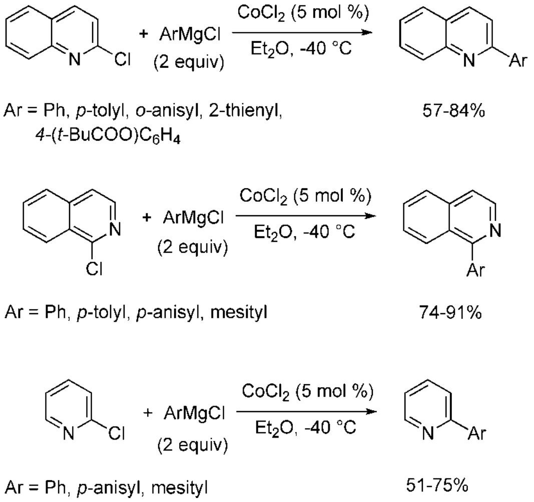
The reaction affords poor yields, and a substantial amount of homocoupling product accruing from the Grignard reagent is produced. The purification of the final product is thus often delicate.

In 2003, Knochel and Cahiez reported the cross-coupling between heteroaryl chlorides and aryl- or heteroarylmagnesium halides[16] (Scheme 10).

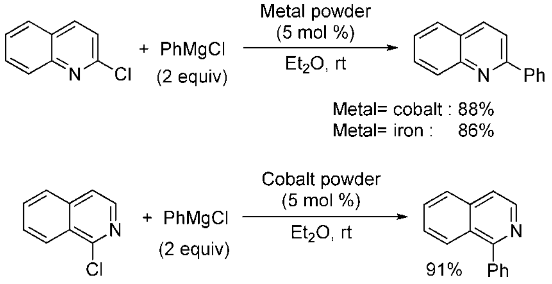
Scheme 9. Cross-coupling between Diaryltellurides and Aromatic Grignard Reagents



Scheme 10. $CoCl_2$-Catalyzed Cross-coupling between Heteroaryl Chlorides and Aromatic or Heteroaromatic Grignard Reagents



Scheme 11. Cobalt or Iron Powder-Mediated Aryl−Aryl Coupling Reactions



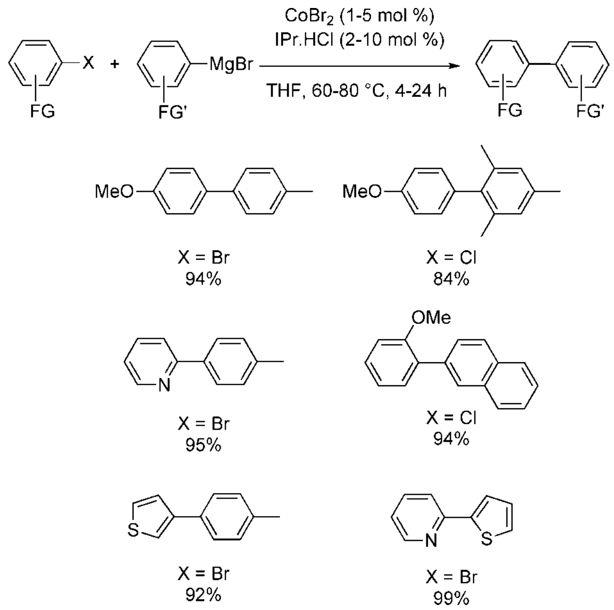
Yields are excellent in most cases. Noteworthy, the influence of steric hindrance is not very important. Thus, the reaction between mesitylmagnesium chloride and 1-chloroisoquinoline leads to 85% of coupling product. Two equivalents of Grignard reagent are required.

Interestingly, cobalt or iron powders are suitable catalysts for the reaction[16] (Scheme 11).

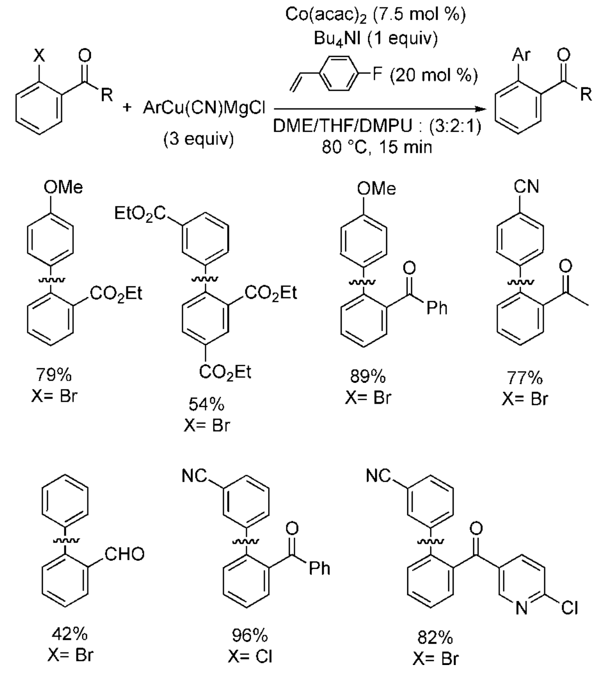
One year later, Oshima[16b] reported a very similar reaction. The coupling is achieved in dioxane in the presence of cobalt(II) acetylacetonate whereas diethyl ether and cobalt(II) chloride were used in the previous method[16a] (Scheme 10). Yields are comparable, but 3 equiv of phenyl magnesium bromide are used instead of 2 and the amount of catalyst is twice higher.

The above examples were performed by using heteroaromatic or actived aromatic halides. Very recently, Nakamura[17] described a cobalt-catalyzed cross-coupling reaction from nonactivated aryl chlorides or heteroaryl bromides and aromatic Grignard reagents (Scheme 12). The reaction is performed in the presence of cobalt(II) fluoride and NHC ligand.

Scheme 12. Cobalt-Catalyzed Cross-coupling between Nonactivated Aryl Halides or Heteroaryl Bromides and Aromatic Grignard Reagents



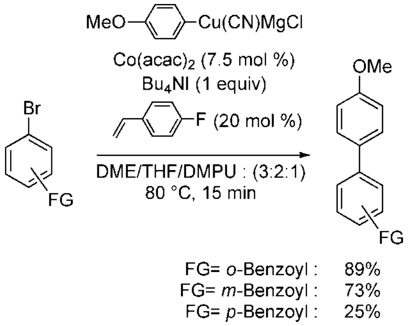
Scheme 13. Cobalt-Catalyzed Cross-coupling between Functionalized Arylcyanocuprates and *ortho*-Bromo or *ortho*-Chloro Aromatic Ketones, Esters, or Aldehydes



Then, Knochel has shown that the chemoselective coupling between polyfunctional aryl- or heteroarylcyanocuprates ArCu(CN)MgCl and *ortho*-bromo or *ortho*-chloro aromatic ketones, esters, or aldehydes can be performed under cobalt catalysis.[18] Numerous polyfunctional biaryls were successfully synthesized according to this methodology. Selected examples are presented in Scheme 13.

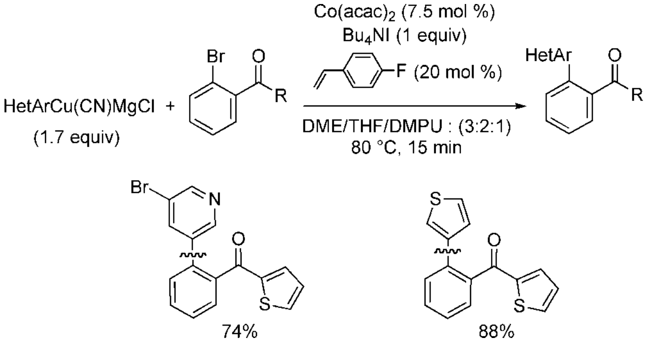
To react the starting halide completely, it is essential to perform the coupling in the presence of Bu_4NI (1 equiv) and 4-fluorostyrene (20 mol %) by using a large excess of cyanoarylcuprate (3 equiv).[19] The use of a THF/DME/DMPU mixture instead of THF as a solvent clearly accelerates the reaction (15 min instead of 21 h).

Scheme 14. Cobalt-Catalyzed Reaction of *p*-Anisylcyanocuprates with *o*-, *m*-, and *p*-Bromobenzophenones

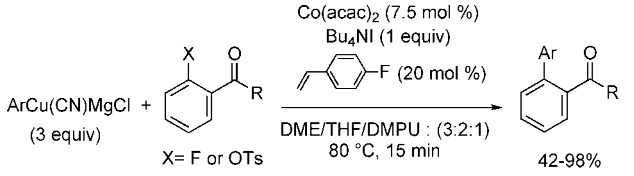


FG= *o*-Benzoyl : 89%
FG= *m*-Benzoyl : 73%
FG= *p*-Benzoyl : 25%

Scheme 15. Cobalt-Catalyzed Cross-coupling between Heteroarylcyanocuprates and Activated Aryl Bromides



Scheme 16. Cobalt-Catalyzed Cross-coupling between Activated Aryl Fluorides or Tosylates and Arylcyanocuprates



The yields are significantly lower when the activating carbonyl group is in the *meta* or the *para* position (Scheme 14).

Heteroarylcyanocuprates can also be used successfully (Scheme 15).

The reaction has been extended to *ortho*-fluoro aromatic ketones, esters, or aldehydes[20] (Scheme 16). The corresponding tosylates also react successfully. This is worthy of note, since the use of aryl fluorides[21] and tosylates[22] in metal-catalyzed cross-coupling reactions is not usual. As a rule, good to excellent yields are obtained.

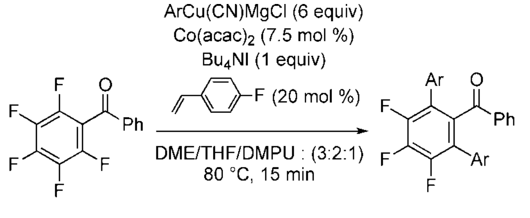
With pentafluorobenzophenone, the two fluorine atoms in the *ortho*-positions can be selectively substituted (Scheme 17). However, yields are moderate and 6 equiv of arylcyanocuprate are required.

3.2.2. From Two Aromatic Halides

Very recently, Gosmini reported the synthesis of unsymmetrical biaryl compounds by coupling two aromatic halides ArX and Ar′X under cobalt catalysis[23] (Scheme 18). The use of 2 equiv of the more reactive aryl halide is generally required to obtain satisfactory yields of cross-coupling products.

Similar results were obtained from aryl iodides, bromides, or chlorides (Table 5). Interestingly, aryl triflates also react successfully (Table 5, entry 7). It should be underlined that a significant amount of homocoupling product is produced during the reaction. This is a practical drawback, since the expected product could then be very tricky to isolate.

Scheme 17. Cobalt-Catalyzed Coupling Reaction between Arylcyanocuprates and Pentafluorobenzophenone



Ar= *m*, *p*-Cl-C_6H_4 : 50%
Ar= *m*-CN-C_6H_4 : 39%

Scheme 18. Synthesis of Unsymmetrical Biaryl Compounds by Coupling Two Aryl Halides under Cobalt Catalysis

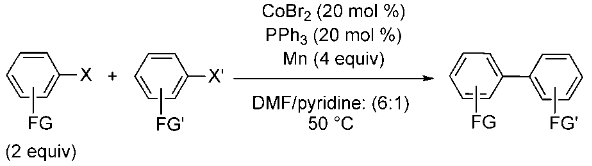
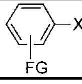
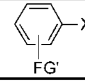
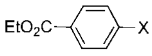
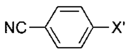
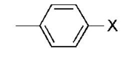
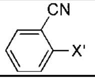
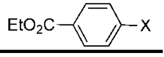
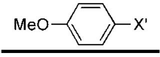
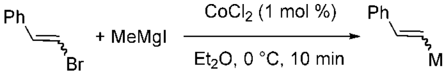


Table 5. Cobalt-Catalyzed Coupling of Two Aryl Halides: Influence of the Nature of the Aryl Halides

Entry		X		X'	Yield (%)[a]
1		I		Br	57 (75)[b]
2		Br		Br	56 (75)[b]
3		Br		Cl	47 (72)[b]
4		I		Br	70 (88)[b]
5		Br		Cl	72
6		Cl		Br	84
7		OTf		Br	86

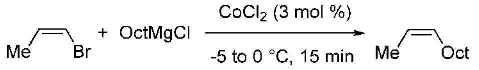
[a] Isolated yield. [b] Yields in parentheses refer to GC yield.

Scheme 19. Cobalt-Catalyzed Coupling Reaction between *β*-Bromostyrene and Methylmagnesium Iodide



75%

Scheme 20. Influence of NMP on the Cobalt-Catalyzed Alkenylation of Grignard Reagents



THF : 45%
THF-NMP (9 equiv) : 88%

4. C_{sp^2}—C_{sp^3} Cross-coupling Reactions

4.1. Alkenylation

4.1.1. From Aliphatic Organometallic Reagents

In 1945, Kharasch[24] showed that the coupling between methyl magnesium iodide and *β*-bromostyrene takes place in good yield in the presence of cobalt chloride (Scheme 19).

Scheme 21. Cobalt-Catalyzed Alkenylation of Grignard Reagents: Stereospecificity of the Reaction

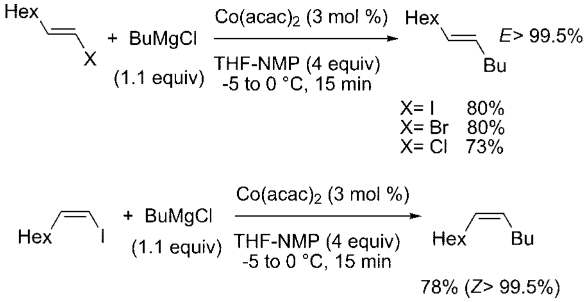
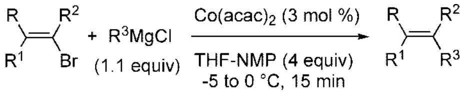
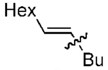
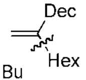
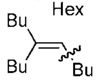
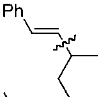
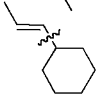
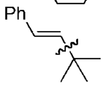
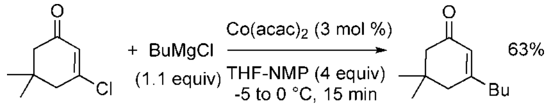


Table 6. Cobalt-Catalyzed Coupling between Alkenyl Halides and Aliphatic Grignard Reagents

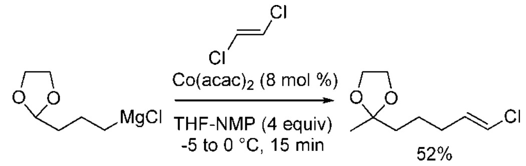


Entry	Product	Yield (%)
1		73
2		73
3		75
4		71
5		87
6		36

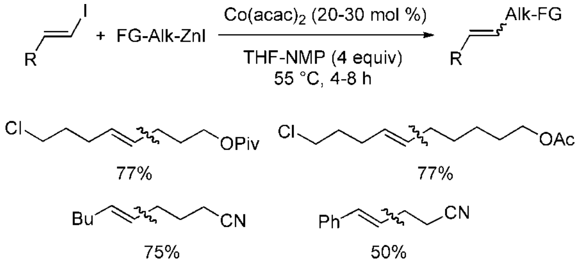
Scheme 22. Chemoselective Cobalt-Catalyzed Alkenylation of Grignard Reagents



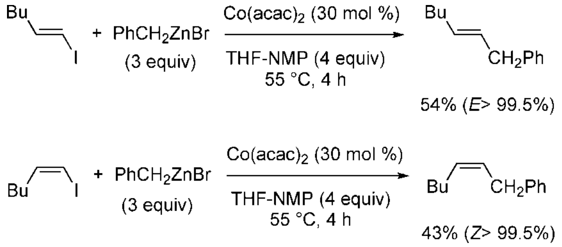
Scheme 23. Synthesis of (*E*)-1-Alkenyl Chlorides from (*E*)-Dichloroethylene



Scheme 24. Cobalt-Catalyzed Alkenylation of Functionalized Organozinc Halides



Scheme 25. Cobalt-Catalyzed Alkenylation of Benzylzinc Bromide



However, the method is limited to the very reactive β-bromostyrene, and 2 equiv of Grignard reagent are necessary.

In 1998, Cahiez discovered that the use of *N*-methylpyrrolidone (NMP) as a cosolvent allows a dramatic improvement (Scheme 20; see also section 3.1). The yields are clearly better, and only 1.1 equiv of Grignard reagent is required.[12]

Alkenyl iodides, bromides, and chlorides give good yields of cross-coupling product (Scheme 21).

It is important to note that the reaction is stereospecific (Scheme 21).

The procedure has been applied to the synthesis of various olefins (Table 6).

Good yields are obtained by coupling primary (Table 6, entries 1−3) or secondary (entries 4−5) aliphatic Grignard reagents with various alkenyl bromides. It is noteworthy that tertiary aliphatic Grignard reagents give poor results (entry 6).

The reaction is highly chemoselective. Thus, the presence of an ester or even a keto group is tolerated (Scheme 22).

Finally, it should be underlined that (*E*)-1,2-dichloroethylene reacts to give only the corresponding (*E*)-alkenyl chlorides. The formation of the product resulting from a substitution of both chlorine atoms is not observed (Scheme 23). This result is in sharp contrast with that obtained under iron catalysis, since, in this case, the double substitution product is formed exclusively.[25]

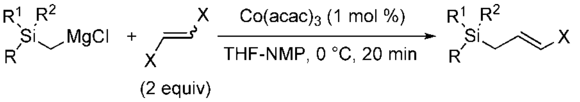
Cahiez and Knochel then extended the reaction to alkylzinc halides.[26] These reagents are less reactive than the corresponding organomagnesium halides, and the coupling takes place slowly at a higher temperature (55 °C, 4−8 h). In addition, 20−30 mol % of catalyst and a large excess of organozinc halide (3 equiv) are necessary. As with Grignard reagents,[12] the reaction is chemoselective and stereospecific. Good yields of cross-coupling product are obtained (Scheme 24).

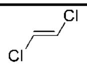
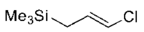
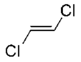
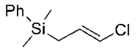
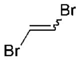
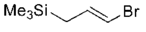
It is worthy of note that benzylic organozinc halides can be coupled with alkenyl iodides (Scheme 25).

The coupling of various silylated Grignard reagents with 1,2-dihalogenoethylenes was also reported (Table 7).[27]

Excellent yields are obtained from trimethylsilylmethylmagnesium chloride (Table 7, entries 1 and 3) or phenyldimethylsilylmethylmagnesium chloride (Table 7, entry 2). As previously reported by Cahiez,[12] the formation of the disubstituted products was not observed. It is noteworthy that stereodifferentiation between (*E*)- and (*Z*)-1,2-dihaloethylenes is possible. Thus, by reacting a mixture of (*E*)- and (*Z*)-1,2-dibromoethylenes (5 equiv) with trimethylsilylmethyl magnesium chloride, the only product is the (*E*)-1-bromoalkene (Table 7, entry 3).

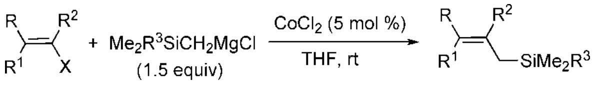
Table 7. Cobalt-Catalyzed Selective Coupling between 1,2-Dihalogenoethylenes and $PhMe_2SiCH_2MgCl$ or Me_3SiCH_2MgCl

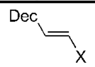
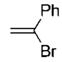
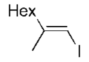
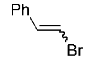
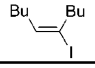


Entry	XCH=CHX	Product	Yield (%)
1			88
2			78
3	 E/Z = 65/35	 E ≈ 100%	74[a]

[a] 5 equiv of 1,2-dibromoethylene was used.

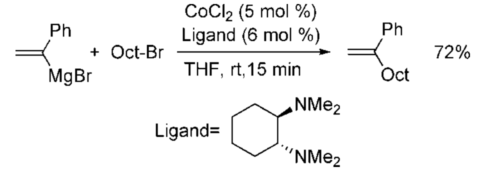
Table 8. Cobalt-Catalyzed Cross-coupling between Alkenyl Halides and Silylated Grignard Reagents



Entry	Alkenyl Halide	X	R^3	Yield (%)
1		I	*i*-PrO	100
2		Br	Me	85
3		Cl	Me	81[a]
4			Me	77
5			Me	74[a]
6	 (E/Z = 6:1)		Me	83 (E/Z = 6:1)
7			Me	25[a]

[a] The reaction was performed at 35 °C.

Scheme 26. Cobalt-Catalyzed Alkylation of Styrylmagnesium Bromide



Later, the cross-coupling between alkenyl halides and dimethylalkylsilylmethylmagnesium chlorides was reported by Oshima.[28] Good to excellent yields are obtained (Table 8).

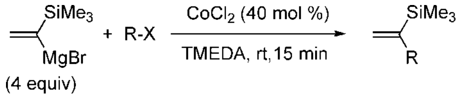
α- or β-monosubstituted as well as β,β-bisubstituted alkenyl iodides, bromides, or chlorides afford good yields (entries 1−6). On the other hand, α,β-bisubstituted alkenyl halides only lead to poor results (entry 7).

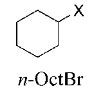
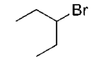
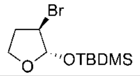
4.1.2. From Aliphatic Halides

In 2006, Oshima[29] described the reaction between octyl bromide and styrylmagnesium bromide in the presence of 5 mol % cobalt chloride and *N*,*N*,*N*′,*N*′-tetramethyl-1,2-cyclohexanediamine as a ligand (Scheme 26).

The same year, he reported the cobalt-catalyzed cross-coupling between various alkyl halides and 1-(trimethylsilyl)ethenylmagnesium bromide by using TMEDA as a solvent.[30] Good to excellent yields are obtained from either primary or secondary alkyl halides, but a large excess of organometallic reagent (4 equiv) has to be used and the reaction seems limited to this specific Grignard reagent (Table 9).

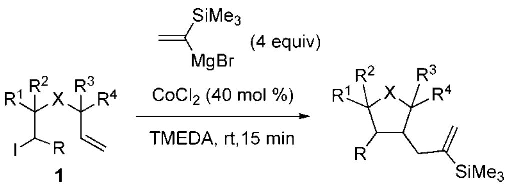
Table 9. Cross-coupling between Primary or Secondary Alkyl Halides and 1-(Trimethylsilyl)ethenylmagnesium Bromide

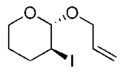
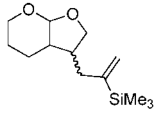
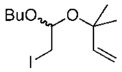
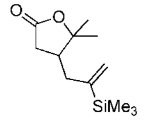
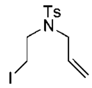


Entry	RX		Yield (%)
1		X= I	87
2		X= Br	85
3		X= Cl	26
4	*n*-OctBr		90
5			64
6			81[a]

[a] The *trans* isomer was formed exclusively.

Table 10. Tandem Radical Cyclization and Cross-coupling Reaction



Entry	1	Product	Yield (%)
1			60 (89/11)[a]
2			78[b]
3			75

[a] Diastereomeric ratio. [b] The product was isolated as a lactone after oxidation of the cyclic acetal.

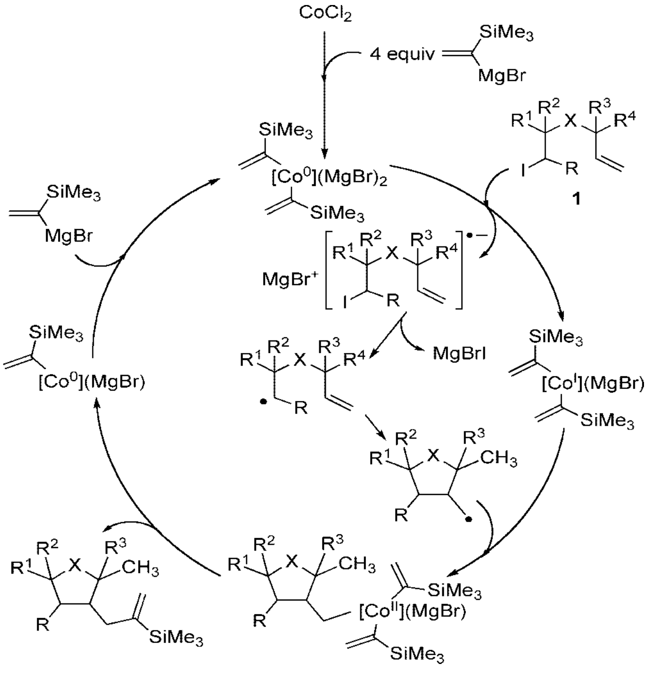
From ε-unsaturated alkyl iodides **1**, a cyclic product is formed via a radical cyclization followed by a cross-coupling reaction (Table 10). The mechanism proposed by Oshima is depicted in Scheme 27. Thus, various heterocyclic compounds have been synthesized in good to excellent yields.

4.2. Arylation

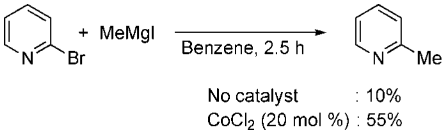
4.2.1. From Aliphatic Halides

The first example of cobalt-catalyzed arylation of a C_{sp^3} center was described in 1969. In this report, Hey[31] noted that the yield of the reaction between 2-bromopyridine and methylmagnesium iodide is clearly improved in the presence of catalytic amounts of cobalt(II) chloride (Scheme 28).

Scheme 27. Mechanism for Tandem Radical Cyclization and Cross-coupling Reaction



Scheme 28. First Cobalt-Catalyzed Arylation of Aliphatic Grignard Reagents



However, the reaction is not general and very poor yields are obtained in most other cases.

In 2001, Oshima[32] described the cobalt-catalyzed tandem radical cyclization and arylation reaction from ethylenic haloacetal **2** (Table 11). This methodology has been applied to the synthesis of heterocyclic (entries 1−7) and carbocyclic (entry 8) compounds. It should be noted that the yield clearly depends on both the position and the number of substituents on the substrate (entries 4 and 6). The mechanism proposed in this case is similar to the one described in Scheme 27.

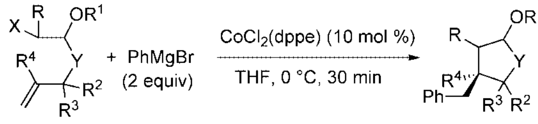
It is noteworthy that when the double bond of the starting product is not terminal (haloacetals **3** and **4**, Scheme 29) the arylation product is not obtained. In this case, the reaction leads to a Heck-type product (see section 9).

In 2006, this reaction was successfully applied to the synthesis of oxasilacyclopentanes (Scheme 30).[33]

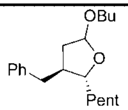
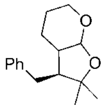
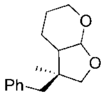
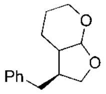
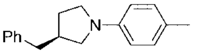
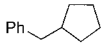
These compounds can easily be converted into 4-aryl-1,3-diols by Tamao−Fleming oxidation.[34] This approach has been used in a synthesis of an antagonist of human CCR5 receptor (Scheme 31).

The same year, Oshima described the cross-coupling between primary alkyl halides and aromatic Grignard reagents in the presence of $CoCl_2(dppp)$.[35] Selected examples are presented in Table 12. It must be underlined that a large excess of Grignard reagent is required (3 equiv). As a rule, moderate yields are obtained from primary alkyl bromides whereas the corresponding iodides give low yields (entries 1 and 2). Moreover, secondary cyclic alkyl bromides such as cyclohexyl bromide lead to poor results (entry 4) and alkyl chlorides do not react.

Table 11. Tandem Radical Cyclization and Cross-coupling Reaction from Unsaturated Haloacetal 2

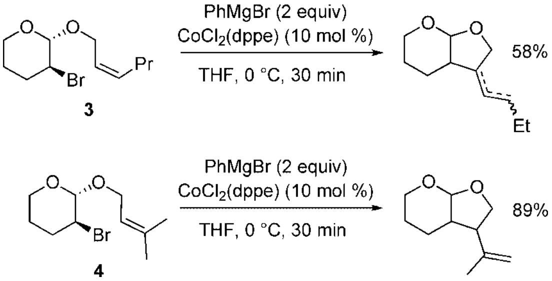


2

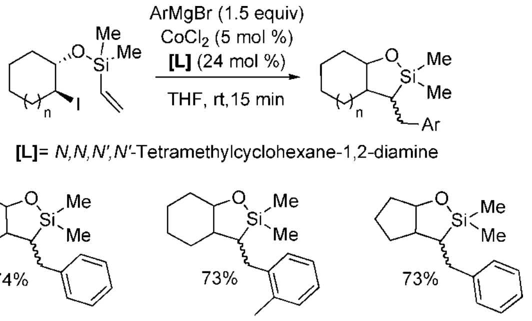
Entry	X	Y	Product	Yield (%)[a]
1	I	O		78 (55/45)
2	Br			80 (55/45)
3	Cl			No reaction
4	Br	O		84 (62/38)
5	Br	O		51 (single)
6	I	O		22 (91/9)
7	I	*p*-Tolyl-N		81
8	I	CH_2		59

[a] Isolated yield. The diastereomeric ratio is given in parentheses.

Scheme 29. Heck-Type Reaction from Unsaturated Haloacetals 3 and 4



Scheme 30. Synthesis of Oxasilacyclopentanes



Heteroaromatic organomagnesium compounds can be used successfully (entry 5). The reaction is sensitive to steric hindrance; thus, *ortho*-substituted aryl Grignard reagents do not afford the expected cross-coupling product (entry 6). Interestingly, some functional groups such as an ester or an acetal are tolerated (entries 7 and 8).

Oshima has finally shown[29] that better results are obtained by using a diamine (*N*,*N*,*N*′,*N*′-tetramethyl-1,2-cyclohexanediamine) as a ligand instead of dppp (Table 13). Moreover, only a slight excess (1.2 equiv) of Grignard

Scheme 31. Synthesis of an Antagonist of Human CCR5 Receptor

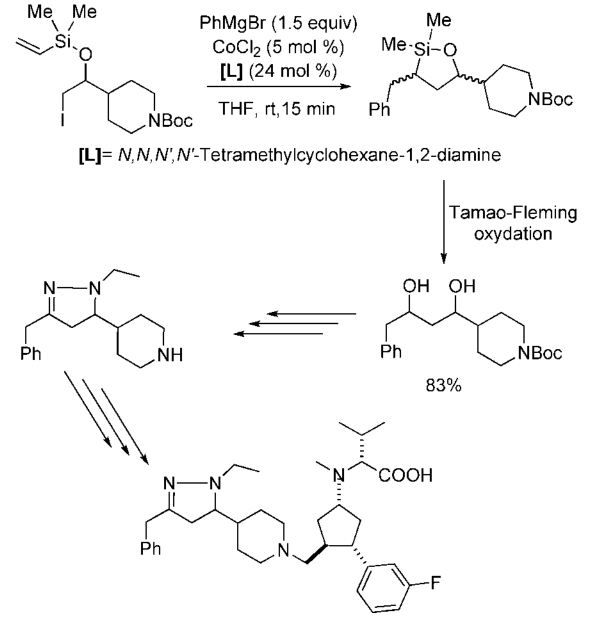
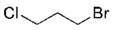
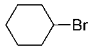
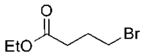
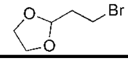


Table 12. Cobalt-Catalyzed Cross-coupling between Primary Alkyl Halides and Aromatic Grignard Reagents

$$\underset{(3\text{ equiv})}{\text{Alk-X + ArMgBr}} \xrightarrow[\text{THF, -15 °C, 30 min}]{\text{CoCl}_2\text{ (10 mol \%)}\ \text{dppp (12 mol \%)}} \text{Alk-Ar}$$

Entry	Alk-X	Ar	Yield (%)
1	*n*-OctBr	Ph	65
2	*n*-OctI	Ph	33
3		Ph	47[a]
4		Ph	24
5	*n*-OctBr	2-Thienyl	54
6		o-Tolyl	<1
7		Ph	49
8		Ph	60

[a] Only 3-chloropropylbenzene is formed.

reagent is then used. With this catalytic system, the yields are significantly higher from primary alkyl iodides than from the corresponding bromides (entries 3 and 4). In addition, secondary cyclic and acyclic alkyl halides (entries 1 and 2) can also be used successfully. Finally, the reaction is less sensitive to steric hindrance; as an example, *ortho*-tolylmagnesium bromide leads to an excellent yield (entry 7).

The reaction is highly chemoselective, and various halogenoesters were coupled successfully (entries 9−11).

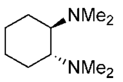
This methodology has been applied to the synthesis of AH13205, a synthetic prostaglandin used as an EP2-receptor agonist that lowers intraocular pressure (Scheme 32).[36]

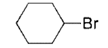
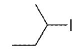
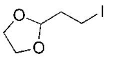
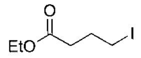
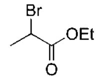
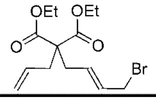
The reaction of five- and six-membered cyclic halo acetals **5** having a stereogenic center in the α position of the C−Br bond has been examined (Scheme 33). The stereoselectivity of this reaction is highly dependent on the size of the ring. Thus, good enantioselectivity was only obtained with the five-membered cyclic acetal.

Table 13. Cobalt-Catalyzed Cross-coupling between Primary or Secondary Alkyl Halides and Aromatic Grignard Reagents

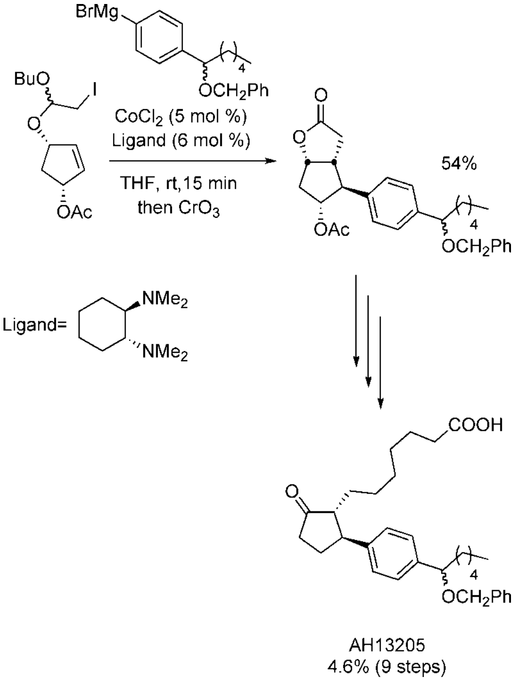
$$\underset{(1.2\text{ equiv})}{\text{Alk-X + ArMgBr}} \xrightarrow[\text{THF, rt,15 min}]{\text{CoCl}_2\text{ (5 mol \%)}\ \text{Ligand (6 mol \%)}} \text{Alk-Ar}$$

Ligand=



Entry	Alk-X	Ar	Yield (%)
1		Ph	95
2		Ph	73
3	*n*-OctI	Ph	99
4	*n*-OctBr	"	80
5	*n*-OctCl	"	10
6	*n*-OctI	2-Thienyl	86
7	*n*-OctI	o-Tolyl	99
8		Ph	86
9		"	91
10		"	88
11		"	56

Scheme 32. Synthesis of AH13205



Very recently, Cahiez[37] described the cobalt-catalyzed cross-coupling between primary or secondary alkyl bromides and aromatic organomagnesium compounds. A cheap and simple catalytic system, cobalt(III) acetylacetonate/TMEDA (1:1), is used. This is very interesting, since commercial TMEDA is a very simple and inexpensive starting material compared to the *N*,*N*,*N*′,*N*′-tetramethyl-1,2-cyclohexanediamine previously employed by Oshima.[29]

It is possible to couple secondary alkyl bromides with excellent yields, whereas, under the conditions described by Oshima,[29] alkyl bromides lead to clearly lower yields than alkyl iodides. This point is very interesting, since alkyl

Scheme 33. Cobalt-Catalyzed Stereoselective Arylation of Cyclic Haloacetals 5

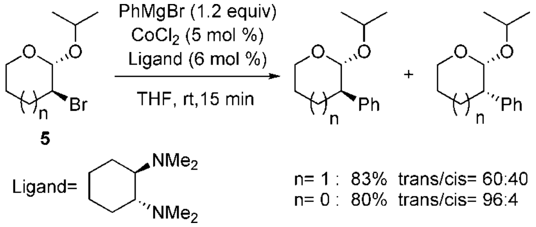
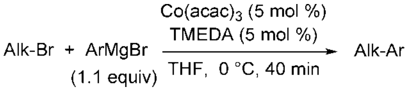
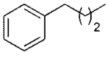
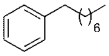
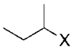
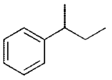
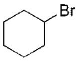
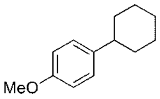
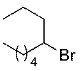
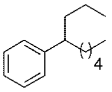
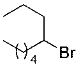
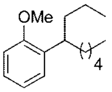
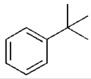


Table 14. Cobalt-Catalyzed Cross-coupling between Aliphatic Bromides and Aromatic Grignard Reagents



Entry	Alk-Br	Product	Yield (%)
1	BuBr		94
2	OctBr		95
3	 X= I		94
4	X= Br		92
5	X= Cl		4
6			97
7			98
8			79
9	*t*-Bu		traces

bromides are cheaper and more stable than the corresponding iodides. Results are summarized in Table 14.

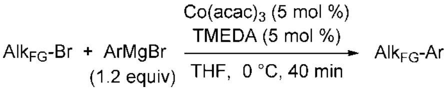
As a rule, excellent yields are obtained from primary and secondary alkyl Grignard reagents (entries 1−8). On the other hand, tertiary alkyl bromides cannot be used (entry 9). It should be underlined that only a slight excess (1.1 equiv) of Grignard reagent was used. Alkyl iodides and bromides lead to similar results (entries 3−4) whereas alkyl chlorides or tosylates only afford poor yields (entry 5).

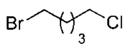
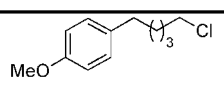
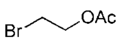
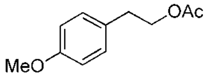
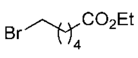
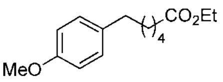
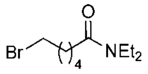
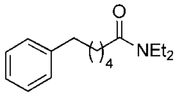
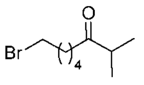
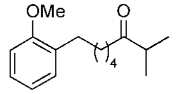
The reaction is not very sensitive to steric hindrance, and it is possible to couple an *ortho*-substituted aromatic Grignard reagent with a secondary alkyl bromide in high yields (entry 8).

The reaction is highly chemoselective (Table 15). Thus, 1-bromo-5-chloropentane couples selectively to give the corresponding alkyl chloride in good yield (entry 1). In addition, the presence of various sensitive groups such as an acetate (entry 2), an ester (entry 3), an amide (entry 4), or even a ketone (entry 5) is tolerated.

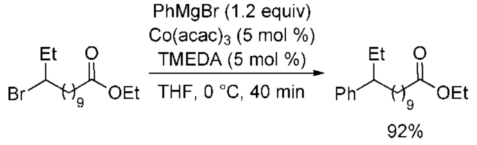
The reaction is also highly chemoselective in the case of secondary alkyl bromides (Scheme 34). It is the first report of a metal-catalyzed cross-coupling between an aromatic Grignard reagent and a functionalized secondary alkyl bromide.

Table 15. Cross-coupling of Aryl Grignard Reagents with Functionalized Primary Alkyl Bromides

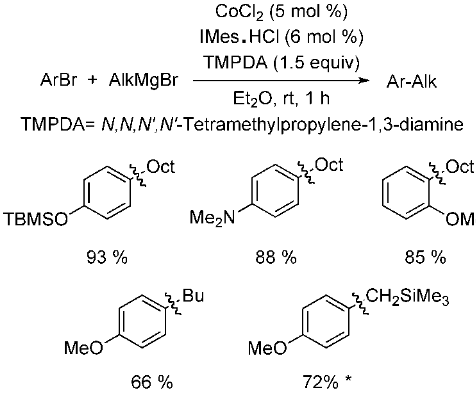


Entry	AlkFG-Br	Product	Yield (%)
1			89
2			88
3			90
4			84
5			88

Scheme 34. Cobalt-Catalyzed Chemoselective Arylation of Functionalized Secondary Alkyl Bromides



Scheme 35. Cobalt-Catalyzed Cross-coupling between Aryl Bromides and Alkyl Grignard Reagents



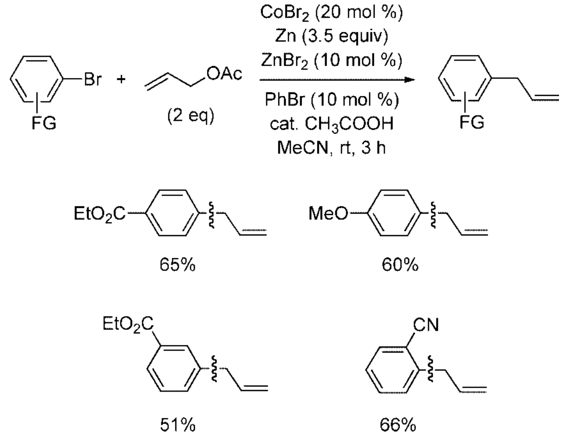
* Reaction performed at reflux for 16 h

4.2.2. From Aromatic Halides

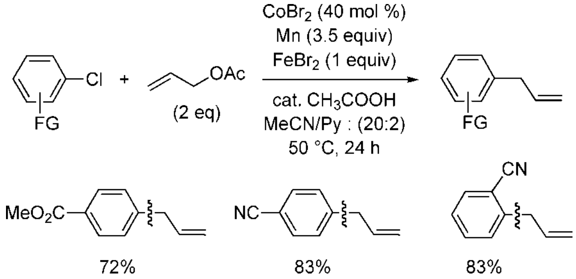
In 2008, Oshima[38] described the cobalt-catalyzed coupling between aryl bromides and aliphatic Grignard reagents (Scheme 35). It is the only report in this field. This reaction is an interesting alternative to the related palladium or nickel procedures.

Yields are generally good to excellent; however, this reaction can only be applied to primary alkyl Grignard reagents.

Scheme 36. Cobalt-Catalyzed Coupling between Allyl Acetate and Functionalized Aryl Bromides



Scheme 37. Cobalt-Catalyzed Coupling between Allyl Acetate and Functionalized Aryl Chlorides



4.3. Allylation of Aromatic Organometallics

In 2003, Périchon reported the coupling of aryl halides with allyl acetates in the presence of a catalytic amount of cobalt bromide; zinc is used as a reductant.[39]

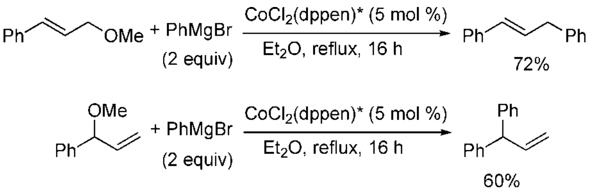
Moderate yields were obtained from various aryl bromides (Scheme 36). It should be noted that the presence of an ester or a nitrile is tolerated. This method is complementary to the cobalt-catalyzed electrochemical methods previously reported.[40]

The reaction can also be achieved with aryl chlorides (Scheme 37), but the reaction conditions are very different. It is necessary to increase the amount of cobalt bromide (40% instead of 20%), zinc dust has to be replaced by manganese dust as a reductant, and the presence of pyridine as well as a stoichiometric amount of iron bromide is required. Moreover, the coupling is performed at a higher temperature (50 °C), and the reaction time is longer (24 h). However, yields are generally better than those previously obtained from the corresponding aryl bromides.

In 2004, Oshima[41] described the reaction between allylic ethers and phenylmagnesium bromide in the presence of cobalt salts. Good yields were obtained, but the reaction is not regioselective, excepted with 1- and 3-phenyl-2-propenyl methyl ethers (Scheme 38).

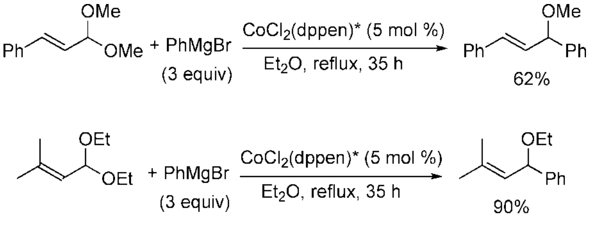
Under similar conditions, allylic acetals lead to the monosubstitution product (Scheme 39).

Scheme 38. Cobalt-Catalyzed Cross-coupling between 1- and 3-Phenyl-2-propenyl Methyl Ethers and Phenylmagnesium Bromide



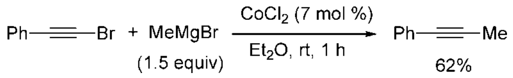
*dppen= 1,5-Bis(diphenylphosphino)pentane

Scheme 39. Cobalt-Catalyzed Arylation of Allylic Acetals



*dppen= 1,5-Bis(diphenylphosphino)pentane

Scheme 40. Cobalt-Catalyzed Coupling between 2-Bromo-1-phenylacetylene and Methylmagnesium Bromide



Scheme 41. Cobalt-Catalyzed Coupling between Phenylethynylmagnesium Bromide and Phenylethynyl Iodide

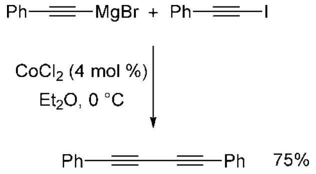
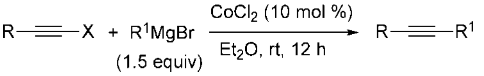


Table 16. Cobalt-Catalyzed Alkynylation of Various Grignard Reagents



Entry	R—≡—X	R^1	Yield (%)
1	Ph—≡—Br	Me	40
2		Bu	32
3		Ph	39
4	Bu—≡—Br	Bu—≡—	28
5	Ph—≡—Br	"	31
6	Ph—≡—I	Ph—≡—	30

5. Alkynylation

5.1. Pioneering Works

In 1945, Kharasch[42] reported the coupling between methylmagnesium bromide and 2-bromo-1-phenylacetylene in the presence of cobalt chloride (Scheme 40). It is the first example of cobalt-catalyzed alkynylation of Grignard reagents.

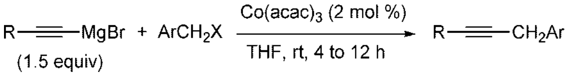
A few years later, the cobalt-catalyzed coupling between phenylethynylmagnesium bromide and phenylethynyl iodide was reported (Scheme 41).[43] A satisfactory yield of diphenylbutadiyne was obtained.

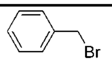
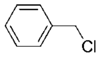
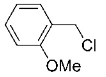
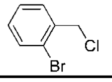
In 1954, several examples of coupling between aliphatic, aromatic, or acetylenic Grignard reagents and 1-haloalkynes were reported by Weedon.[44] As a rule, only poor yields were obtained (Table 16).

5.2. Benzylation of Acetylenic Grignard Reagents

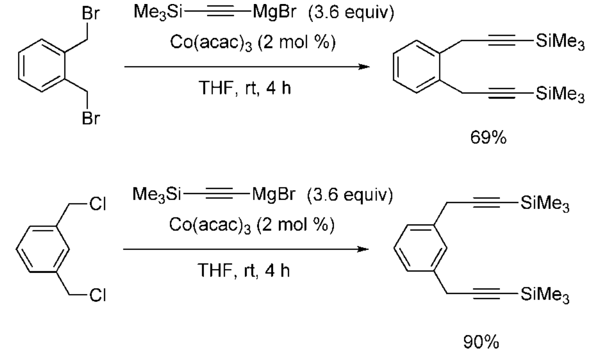
In 2006, Oshima reported the benzylation of acetylenic Grignard reagents under cobalt catalysis.[45] Moderate to excellent yields are obtained (Table 17).

Table 17. Cobalt-Catalyzed Benzylation of Alkynylmagnesium Halides



Entry	ArCH$_2$X	Yield (%) R= n-Bu	Yield (%) R= SiMe$_3$
1		70	71
2		21	82
3		-	93
4		31	40

Scheme 42. Preparation of Diynes from 1,2-Bis(bromomethyl)- or 1,3-Bis(chloromethyl)benzene



Scheme 43. Cobalt-Catalyzed Cross-coupling between Primary or Secondary Alkyl Bromides and 1-Trimethylsilylethynylmagnesium Bromide

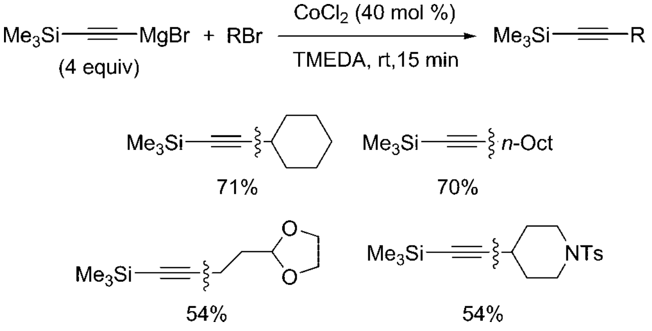
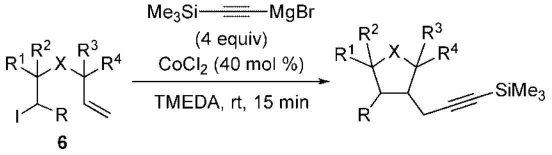
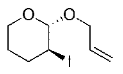
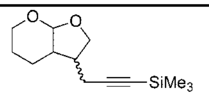
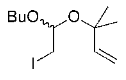
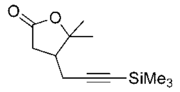
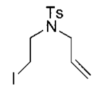
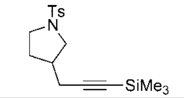


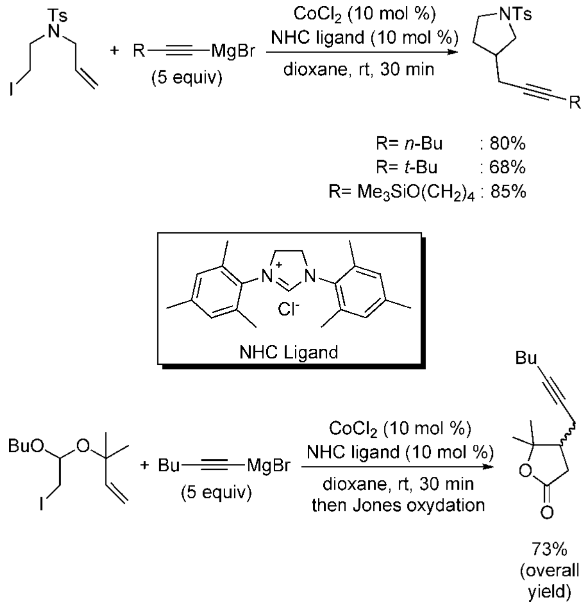
Table 18. Cobalt-Catalyzed Tandem Radical Cyclization and Alkynylation Reaction



Entry	Compound 6	Product	Yield (%)
1			44 (89/11)[a]
2			66[b]
3			68

[a] Diastereomeric ratio. [b] The product was isolated as a lactone after oxidation of the cyclic acetal.

Scheme 44. Cobalt-Catalyzed Tandem Radical Cyclization and Alkynylation Reaction



Trimethylsilylethynylmagnesium bromide reacts with benzylic chlorides or bromides to give good yields of cross-coupling products (entries 1−4, R = Me$_3$Si). On the other hand, only benzylic bromides lead to good results from 1-hexynylmagnesium bromide (entry 1, R = *n*-Bu).

With 1,2-bis(bromomethyl)- or 1,3-bis(chloromethyl)benzene, the double substitution is possible and the reaction affords diynes (Scheme 42).

5.3. Alkylation of Acetylenic Grignard Reagents

Recently, Oshima reported the reaction between alkyl halides and trimethylsilylethynylmagnesium bromide in the presence of cobalt chloride.[29] Satisfactory yields are obtained from primary or secondary alkyl halides (Scheme 43), but a large excess of Grignard reagent is used.

ε-Haloalkenes **6** react with trimethylsilylethynylmagnesium bromide according to a tandem radical cyclization and cross-coupling reaction. Various heterocyclic compounds have thus been synthesized in moderate to good yields (Table 18).

Oshima[46] showed that simple acetylenic Grignard reagents can also be used (Scheme 44).

However, it is important to note that 5 equiv of Grignard reagent have to be used in this case.

5.4. Alkenylation of Acetylenic Grignard Reagents

The cobalt-catalyzed coupling between alkynylmagnesium halides and alkenyl triflates was described by Hayashi in 2007.[47] Good to excellent yields are obtained from a wide range of substrates (Scheme 45).

Some examples of chemoselective couplings in the presence of an alkenyl, an alkyl, or an aryl bromide are described (Table 19). It is noteworthy that no additional ligand was used in this case.

Scheme 45. Cobalt-Catalyzed Coupling between Alkenyl Triflates and Alkynyl Grignard Reagents

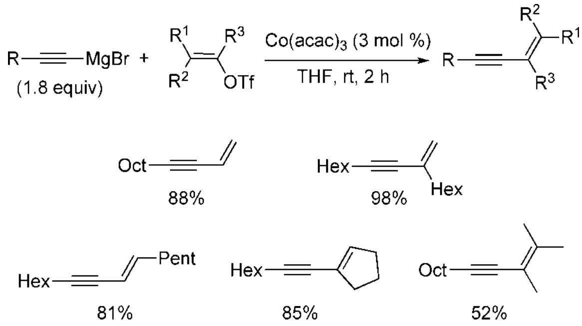
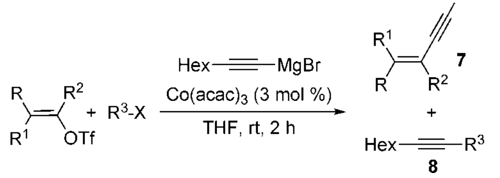
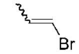
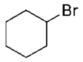
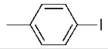
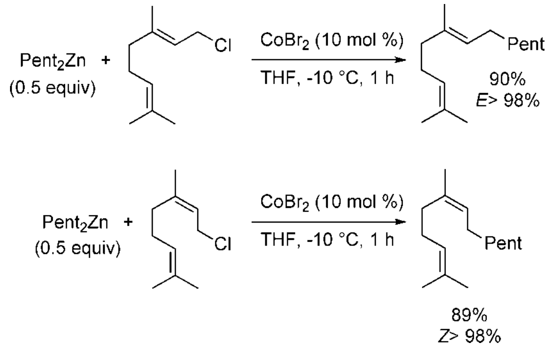


Table 19. Chemoselective Cobalt-Catalyzed Alkenylation of Acetylenic Grignard Reagents



Entry	R^3-X	Selectivity (**7**:**8**)	Yield (%)
1		89:11	68
2		> 99:1	60
3		> 99:1	50

Scheme 46. Cobalt-Catalyzed Allylation of Diorganozinc Compounds



6. C_{sp^3}—C_{sp^3} Cross-coupling

6.1. Allylation

6.1.1. Allylation of Aliphatic Organozinc Compounds

In 1996, Knochel[48] described the allylation of organozinc compounds (R_2Zn or RZnX) under cobalt catalysis (Scheme 46).

It should be pointed out that both R groups from R_2Zn are transferred. Moreover, only the SN_2 substitution products are obtained. Dialkylzincs and alkylzinc halides give similar yields, but the latter require longer reaction times (about 5 h at −10 °C).

Allylic phosphates can also be used successfully (Scheme 47).

6.1.2. Alkylation of Allylic Grignard Reagents

The coupling between unactivated alkyl halides and allylic Grignard reagents in the presence of cobalt chloride and dppp was described by Oshima in 2002 (Table 20).[49] Good yields are obtained under mild conditions from primary (entry 1), secondary (entries 2 and 3), or tertiary (entries 4 and 5) alkyl halides. Benzylic halides can also be used (entry 6).

Scheme 47. Cobalt-Catalyzed Coupling between Diethyl Cinnamyl Phosphate and Dipentylzinc

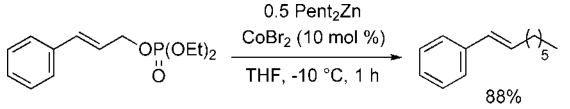
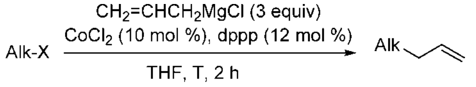
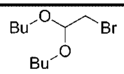
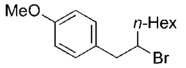
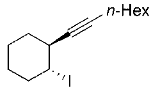
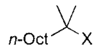
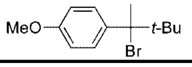


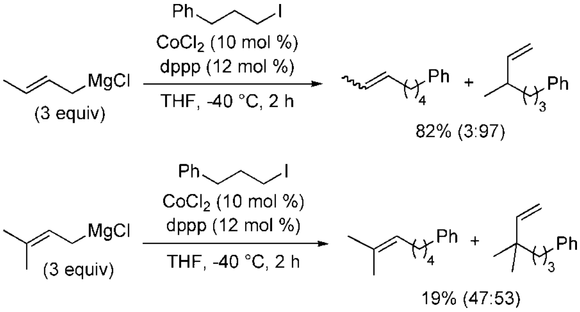
Table 20. Cobalt-Catalyzed Coupling between Unactivated Alkyl Halides and Allylmagnesium Chloride



Entry	Alk-X	T (°C)	Yield (%)
1		-40	82
2		-20	84
3		-40	76[a]
4	 X= Br	-20	90
5	X= Cl	20	31
6		-20	73[b]

[a] *trans/cis* = 86:14. [b] dppe was used as a ligand.

Scheme 48. Cobalt-Catalyzed Alkylation of Crotyl- and Prenylmagnesium Chlorides



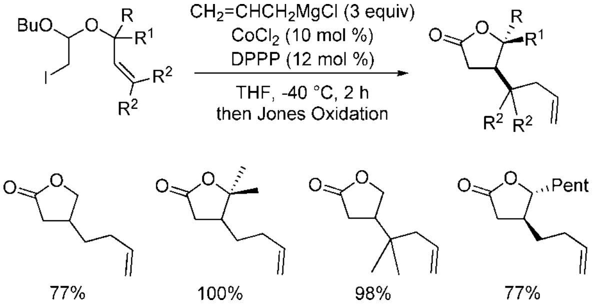
With substituted allylic Grignard reagents, the regioselectivity is very dependent on the structure of the allylic moiety. A mixture of products resulting from an alkylation on the less and the more substituted sides of the allylic system is generally obtained (Scheme 48).

A tandem radical cyclization and cross-coupling reaction was used to prepare various cyclic compounds in good to excellent yields (Scheme 49). For the mechanism of the reaction, see Scheme 27.

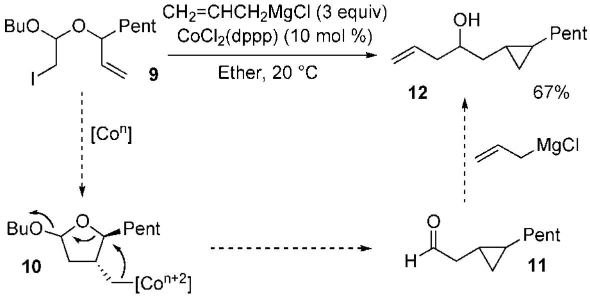
Unexpectedly, by using ether as a solvent, a cyclopropane derivative is formed (Scheme 50).

The following mechanism is proposed. At first, cobalt chloride is converted to an active reduced species [Co^n] by action of the Grignard reagent. After a single electron transfer to the halide (formation of a radical anion) and then cleavage of the C−I bond, a radical is obtained. Sequential 5-exo radical cyclization and trapping of the resulting radical by the catalytic cobalt species then afford the cobalt intermediate **10**. In diethyl ether, **10** undergoes

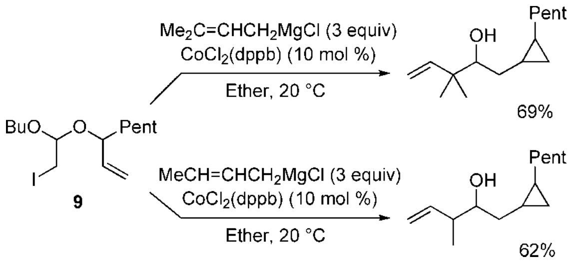
Scheme 49. Cobalt-Catalyzed Tandem Radical Cyclization and Alkylation of Allylic Grignard Reagents



Scheme 50. Mechanism of the Cobalt-Catalyzed Reaction of δ-Iodoallylic Acetal 9 with Allylmagnesium Chloride



Scheme 51. Cobalt-Catalyzed Reaction of δ-Iodoallylic Acetal 9 with Crotyl- and Prenylmagnesium Chlorides



a rapid elimination of BuO-Metal (Metal = Co or Mg) to give the cyclopropane derivative **11**. Such an elimination probably involves the complexation of the metallic center of **10** (Co or Mg) with the oxygen atom of the butoxy group (in THF, this complexation is much more difficult and the elimination does not occur). The resulting aldehyde **11** then reacts with allylmagnesium chloride to afford the alcohol **12**.

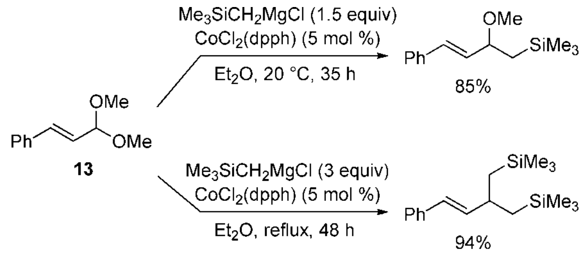
The reaction was extended to prenyl- or crotylmagnesium chlorides (Scheme 51).

6.1.3. Allylation of Trimethylsilylmethylmagnesium Chloride

The coupling between allylic ethers and trimethylsilylmethylmagnesium chloride under cobalt catalysis was reported in 2004.[41] As with phenylmagnesium bromide (see section 4.3), good yields and selectivity are obtained from 1- and 3-phenyl-2-propenyl methyl ethers (Scheme 52). However, the reaction is generally not regioselective with the other allylic ethers.

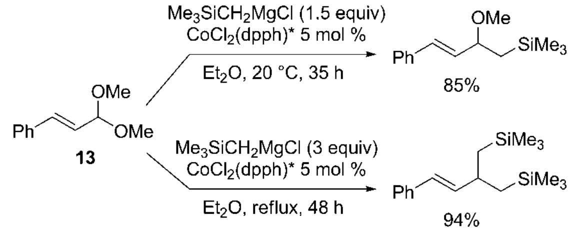
It is noteworthy that, from allylic acetals **13** (Scheme 53), it is possible to substitute one or two methoxy groups by using respectively 1.5 or 3 equiv of Grignard reagent.

Scheme 52. Cobalt-Catalyzed Cross-coupling between 1- and 3-Phenyl-2-propenyl Methyl Ethers and Trimethylsilylmethylmagnesium Chloride



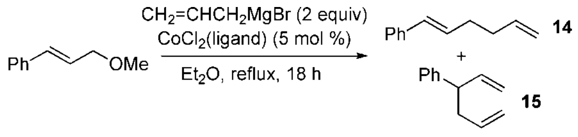
*dpph= 1,6-Bis(diphenylphosphino)hexane

Scheme 53. Cobalt-Catalyzed Coupling of Allylic Acetals with Trimethylsilylmethylmagnesium Chloride



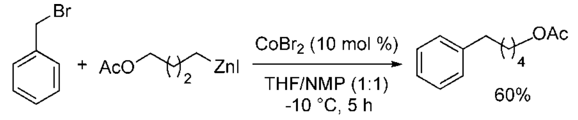
*dpph= 1,6-Bis(diphenylphosphino)hexane

Scheme 54. Cobalt-Catalyzed Coupling between Allylmagnesium Bromide and Cinnamyl Methyl Ether



No ligand : 78% **14/15** > 99:1
dppp : 70% **14/15** = 30:70

Scheme 55. Cobalt-Catalyzed Benzylation of 4-Acetoxybutylzinc Iodide



6.1.4. Allylation of Allylic Grignard Reagents

A cobalt-catalyzed coupling reaction between allylic Grignard reagents and allylic ethers has been described by Oshima (Scheme 54).[41]

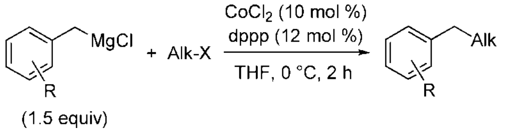
Good yields are obtained. Interestingly, the regioselectivity of the reaction can be easily controlled by changing the nature of the catalyst. Thus, only the linear substitution product **14** is formed in the presence of uncomplexed cobalt chloride whereas the branched substitution product **15** is the main isomer when the complex $CoCl_2$•dppp is used.

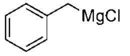
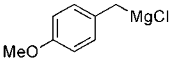
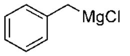
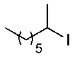
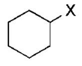
6.2. Benzylation

An example of cobalt-catalyzed benzylation of an organozinc compound (Scheme 55) was reported by Knochel in1996.[48]

In 2004, Oshima achieved the coupling between secondary alkyl halides and benzylic Grignard reagents in the presence of $CoCl_2$•dppp. As a rule, yields are moderate (Table 21).[49] Tertiary alkyl iodides also react but lead to poor yields (entry 7).

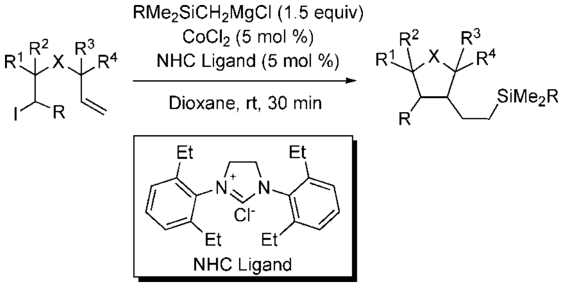
Table 21. Cobalt-Catalyzed Alkylation of Benzylic Grignard Reagents

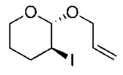
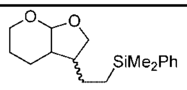
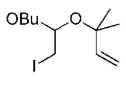
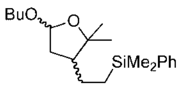
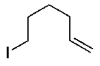
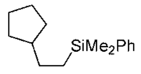
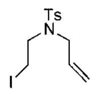
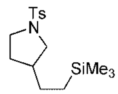
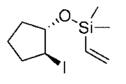
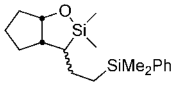


Entry	Grignard Reagent	Alk-X		Yield (%)
1		*s*-BuBr		70
2		"		50
4				62
5	"		X= Br	40
6	"		X= I	61[a]
7	"	*t*-BuI		37

[a] 3 equiv of Grignard reagent was used.

Table 22. Cobalt-Catalyzed Tandem Radical Cyclization and Alkylation Reaction of Various δ-Iodo Ethylenic Compounds with RMe_2SiCH_2MgCl



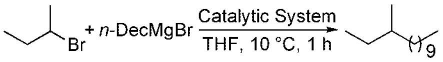
Entry	RI	Product	Yield (%)
1			72 (85/15)[a]
2			81 (67/33)[a]
3			67
4			81
5			65

[a] Diastereomeric ratio.

6.3. Alkylation

In 2007, Oshima reported the tandem radical cyclization and cross-coupling reaction of various δ-halogeno ethylenic compounds with RMe_2SiCH_2MgCl under cobalt catalysis.[46] *N*-Heterocyclic carbenes are employed as ligands. As a rule, good yields are obtained under mild conditions. Selected examples are shown in Table 22.

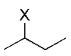
Table 23. Cobalt-Catalyzed Alkyl−Alkyl Coupling Reaction: Effect of Iodide Anion on the Course of the Reaction



Entry	Catalytic system (5 mol %)	Yield (%)
1	$CoCl_2$	traces
2	$CoCl_2$; 4TMEDA	35
3	$CoCl_2$•2LiCl; 4TMEDA	27
4	$CoCl_2$•2LiBr; 4TMEDA	30
5	$CoCl_2$•2LiI; 4TMEDA	79

Table 24. Cobalt-Catalyzed Coupling between Unactivated Alkyl Halides and Aliphatic Grignard Reagents

$$RBr + R^1MgBr \xrightarrow[\text{THF, 10 °C, 1 h}]{\text{CoCl}_2\text{•2LiI; 4 TMEDA (5 mol \%)}} R\text{-}R^1$$

Entry	RBr		R^1	Yield (%)
1	i-PrBr		n-Dec	89
2		X = Cl	n-Dec	≤ 1
3		X = Br		79
4		X = I		65
5	2-PentBr		n-Oct	62
6	3-PentBr		n-Dec	45
7	2-HeptBr		n-Dec	47
8	c-HexBr		n-Oct	87
9	n-OctBr		n-Pent	97
10	n-BuBr		$BrMgO(CH_2)_8$	70
11	t-PentBr		n-Oct	0
12	n-DecBr		s-Bu	20[a]
13	n-DecBr		t-Bu	0[a]

[a] A mixture of decane and 1-decene was mainly obtained.

Very recently, Cahiez described the cross-coupling between functionalized alkyl halides and aliphatic Grignard reagents in the presence of the ate complex $CoCl_2$•2LiI.[50] TMEDA is used as a ligand.

By using cobalt chloride as a catalyst, only traces of cross-coupling product are obtained (Table 23, entry 1). In the presence of TMEDA, the yield is better but remains unsatisfactory (entry 2). Finally, the best results are obtained by adding both TMEDA and lithium iodide (entry 5). It is the first example of such a beneficial influence of iodide anion on the course of a cobalt-catalyzed cross-coupling reaction.

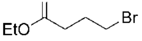
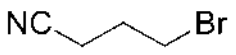
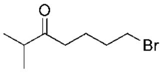
Various alkyl−alkyl couplings were performed under these conditions (Table 24). Acyclic or cyclic secondary alkyl bromides (entries 1−8) gave moderate to good yields of cross-coupling product. It is important to note that the influence of steric effects is determinant. Thus, 2-bromopentane gave a better yield than 3-bromopentane (entries 5 and 6). Similarly, the results obtained with various 2-bromoalkanes clearly depend on the length of the alkyl chain (entries 1, 3, and 7). It is possible to use alkyl iodides in place of bromides, but the corresponding chlorides do not react (entries 2−4).

The reaction has been successfully extended to primary alkyl bromides (entries 9 and 10). On the other hand, tertiary alkyl bromides do not react (entry 11). Finally, it should be noted that secondary or tertiary alkyl Grignard reagents cannot be used (entries 12 and 13).

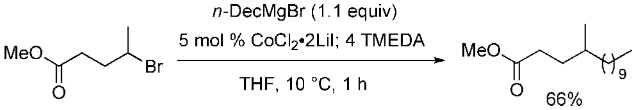
The reaction is chemoselective (Table 25), thus, an ester (entries 1 and 2), a nitrile (entry 3), or even a keto group (entry 4) are tolerated. It should be underlined that func-

Table 25. Cobalt-Catalyzed Coupling between Functionalized Alkyl Halides and Aliphatic Grignard Reagents

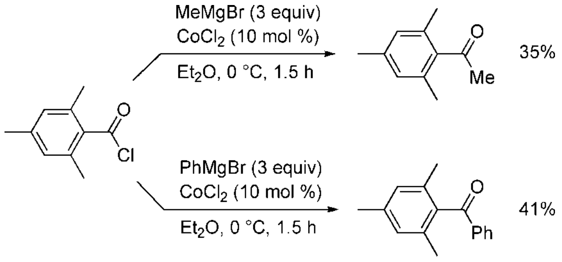
$$R_{FG}\text{-Br} + R^1\text{MgBr} \xrightarrow[\text{THF, 10 °C, 1 h}]{\text{CoCl}_2\bullet 2\text{LiI; 4 TMEDA (5 mol \%)}} R_{FG}\text{-}R^2$$

Entry	R_{FG}-Br	R^1	Yield (%)
1		Et	78
2		*n*-Dec	75
3		*n*-Bu	82
4		*n*-Pent	73

Scheme 56. Cobalt-Catalyzed Chemoselective Alkyl−Alkyl Coupling Reaction from Functionalized Secondary Alkyl Halides



Scheme 57. Cobalt-Catalyzed Acylation of Methyl- and Phenylmagnesium Bromides



tionalized secondary alkyl halides can also be used successfully (Scheme 56).

It is the first example of chemoselective alkyl−alkyl coupling from a functionalized secondary alkyl bromide.

7. Acylation

7.1. From Organometallic Compounds

In 1943, Kharasch showed that methyl- or phenylmagnesium bromides react with mesitoyl chloride in the presence of cobalt chloride to give the expected ketones in moderate yields (Scheme 57).[51] It is the first report of a cobalt-catalyzed acylation of organometallic compounds.

Fifty years later, Knochel showed that diorganozincs react with carboxylic acid chlorides in the presence of cobalt bromide in a THF/NMP mixture as a solvent (Scheme 58).[48]

Excellent yields are obtained with aromatic and aliphatic carboxylic acid chlorides as well as with oxalyl chloride and trifluoroacetic anhydride. It is however important to note that three equivalents of diorganozinc compound have to be used (i.e., 6 equiv of organometallic reagent).

7.2. Cobalt-Mediated Acylation of Aryl Bromides

The cobalt-mediated synthesis of aromatic ketones from aryl bromides and carboxylic acid anhydrides was reported by Périchon[52] in 2004 (Table 26). The reaction is performed in the presence of a catalytic amount of cobalt bromide by using a stoichiometric amount of zinc as a reductant.

Scheme 58. Cobalt-Catalyzed Acylation of Diorganozincs

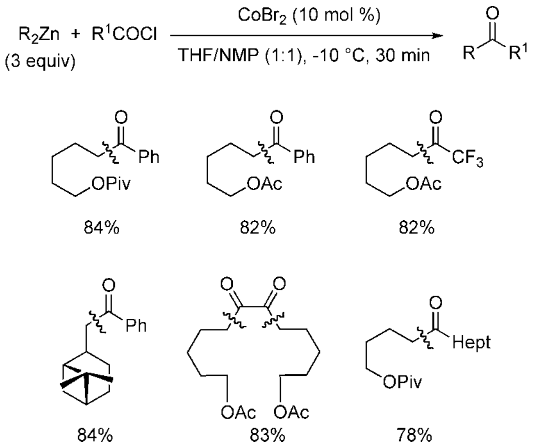
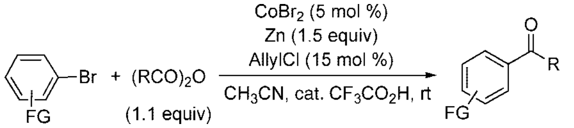


Table 26. Cobalt-Mediated Reaction between Aryl Bromides and Carboxylic Acid Anhydrides



Entry	Aryl bromide	R	Yield (%)
1	*p*-MeO−C_6H_4Br	Me	67
2	*p*-MeO−C_6H_4Br	*n*-Bu	79
3	*p*-MeO−C_6H_4Br	Ph	46
4	*p*-NC−C_6H_4Br	Me	54
5	*p*-NC−C_6H_4Br	*n*-Bu	76
6	*p*-NC−C_6H_4Br	Ph	30[a]
7	*p*-EtO_2C−C_6H_4Br	Me	62
8	*p*-EtO_2C−C_6H_4Br	*n*-Bu	78
9	*p*-EtO_2C−C_6H_4Br	Ph	33[b]
10	*p*-F−C_6H_4Br	Me	69[a]
11	*p*-F_3C−C_6H_4Br	Me	61[a]
12	*m*-MeO−C_6H_4Br	Me	72
13	*m*-NC−C_6H_4Br	Me	34[b]
14	*m*-F_3C−C_6H_4Br	Me	71[a]

[a] 10 mol % $CoBr_2$ was used. [b] 7.5 mol % $CoBr_2$ was used.

Various *para*- (entries 1−11) or *meta*-substituted (entries 12−14) functionalized aryl bromides react successfully. As a rule, aliphatic acid anhydrides give good results whereas aromatic acid anhydrides only lead to moderate yields (entries 3, 6, and 9).

8. Reductive Cyclization and Heck-Type Reactions

8.1. Radical Cyclization

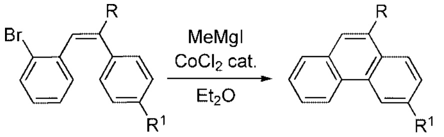
It is well-known that various cobalt(II) complexes react with alkyl or aryl halides via a halogen atom transfer to lead to the corresponding alkyl or aryl radicals.[53,54] Cyclization via an inter- or an intramolecular trapping of the radical thus generated provides an easy access to various cyclic compounds.

8.1.1. Intramolecular Radical Cyclization

8.1.1.1. Radical-Mediated Aryl−Aryl Coupling. Cobalt-catalyzed reductive cyclization has been reported for the first time by Tiecco[55] in 1965 (Scheme 59).

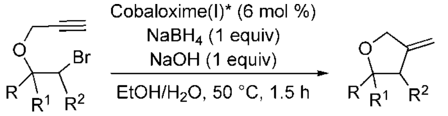
8.1.1.2. From δ-Halogeno Acetylenic Compounds. In 1982, Tada[56] reported the reductive cyclization of 2-propargyloxyalkyl bromides in the presence of bis(dimethylgly-

Scheme 59. Cobalt-Catalyzed Cyclization via a Radical-Mediated Aryl−Aryl Coupling



R= R_1= H : 75%
R= H, R^1= Me : 78%
R= H, R^1= OMe : 85%
R= Ph, R^1= H : 75%

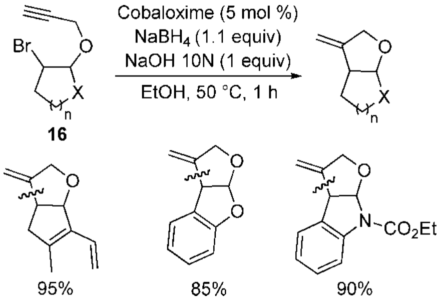
Table 27. Cobaloxime(I)-Catalyzed Reductive Cyclization of 2-Propargyloxyalkyl Bromides



Entry	R	R^1	R^2	Yield (%)
1	Ph	Ph	H	85
2	Ph	Me	H	73
3	Ph	H	H	78
4	H	-$(CH_2)_4$-	64	
5	H	-$(CH_2)_3$-	48	

* Cobaloxime(I) = [bis(dimethylglyoximato)(pyridine)cobalt(I)].

Scheme 60. Cobaloxime(I)-Catalyzed Reductive Cyclization of Halogeno Propargyl Acetals 16



oximato)(pyridine)cobalt(I), generally called cobaloxime(I), by using a stoichiometric amount of sodium borohydride as a reductant. Results are reported in Table 27.

Good yields of exomethylenefuranes are obtained from primary alkyl halides (entries 1−3). Cyclic alkyl halides lead to bicyclic compounds in satisfactory yields (entries 4 and 5).

In 1989, Hoffmann[57] applied the reaction to the synthesis of various heterocyclic compounds (Scheme 60).

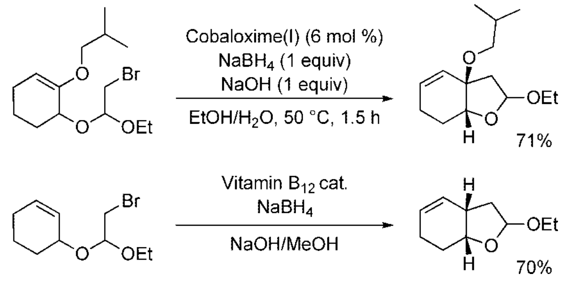
8.1.1.3. From δ-Halogeno Ethylenic Compounds.

In 1984, Pattenden[58] described the radical cyclization of 2-allyloxyalkyl bromides using cobaloxime or Vitamin B12[59] as a catalyst under the conditions described by Tada (Table 27) for 2-propargyloxyalkyl bromides.[56] The organocobalt species resulting from the cyclization undergoes a β-hydrogen elimination to give a bicyclic product in good yields (Scheme 61).

A few years later, Jones[60] reported a similar reaction catalyzed by a cobalt-salen complex. A mixture of saturated and unsaturated products **17** and **18** is obtained in all cases (Scheme 62).

Thereafter, Giese[61] showed that it is possible to form selectively the saturated or the unsaturated products **19** and **20** by changing the reaction conditions (Table 28).

Scheme 61. Cobaloxime(I)- or Vitamin B_{12}-Catalyzed Radical Cyclization of 2-Allyloxyalkyl Bromides



Scheme 62. Radical Cyclization Catalyzed by Cobalt(I)-Salen

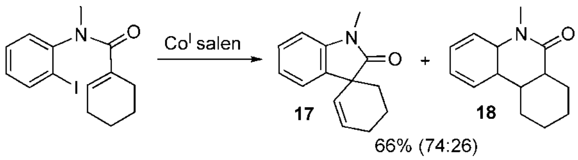
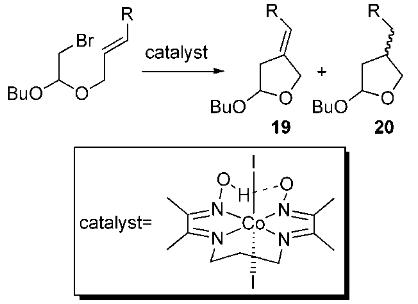
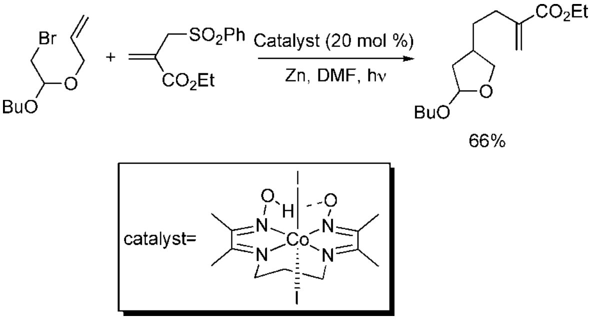


Table 28. Radical Cyclization Catalyzed by Cobalt(I)-Salen: Influence of the Nature of the Reducing System on the Outcome of the Reaction



		Ratio **19/20** (yield %)	
		Reaction conditions	
Entry	R	20 mol % catalyst, Zn, DMF, *hν*	1 mol % catalyst, Zn/NH_4Cl, DMF
1	H	81/19(80)	1/99(80)
2	Ph	99/1 (90)	3/97(88)

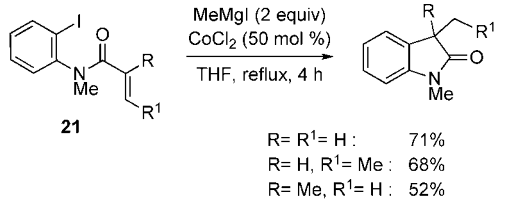
Scheme 63. Tandem Radical Cyclization and Michael Addition Reaction



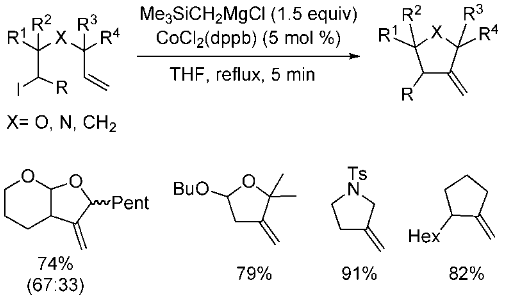
Interestingly, the radical (or the organocobalt species) obtained after the cyclization step can be trapped by using a reactive Michael acceptor such as an acrylic ester (Scheme 63).[61]

In 1994, Jones[62] performed the reductive cyclization of *ortho*-amidoiodobenzenes **21** in moderate to good yields in the presence of cobalt chloride by using methylmagnesium iodide as a reductant (Scheme 64). A large amount of catalyst is required (50 mol %).

Scheme 64. Cobalt-Catalyzed Radical Cyclization of *ortho*-Amidoiodobenzenes 21



Scheme 65. CoCl$_2$•dppb-Catalyzed Radical Cyclization of *δ*-Halogeno Ethylenic Compounds



It is possible to lower the amount of catalyst by using a complex cobalt CoCl$_2$(dppb). Thus, Oshima[63] achieved the radical cyclization of *δ*-halogeno ethylenic compounds in the presence of CoCl$_2$(dppb) by using trimethylsilylmethylmagnesium chloride as a reductant (Scheme 65). Various cyclopentane derivatives were prepared in good yields.

8.1.2. Cyclization via an Intermolecular Radical Addition

In 2003, Cheng[64] reported the reaction of various *o*-iodoaryl ketones and aldehydes with alkynes or conjugated alkenes in the presence of CoI$_2$•dppe and a stoichiometric amount of zinc as a reductant. The cyclization reaction proceeds via a tandem carbometalation and intramolecular 1,2-addition to the ketone.

Such a reaction had been previously described under palladium[65] or nickel[66] catalysis. Nevertheless, the cobalt-catalyzed reaction gives higher yields and better regioselectivities under milder conditions. In addition, the reaction times are shorter (Table 29).

Good to excellent yields are obtained from *o*-iodoaryl ketones (Table 29, entries 1−5) or aldehydes (entries 6−9). When unsymmetrical alkynes are used, a mixture of two regioisomers **22** and **23** is obtained (entries 2 and 7). Interestingly, with trimethylsilylpropyne or ethyl trimethylsilylpropiolate, the regioselectivity is excellent, since only compound **22** is formed (entries 3−5 and 8).

A similar reaction takes place by using various acrylic esters instead of alkynes (Table 30).

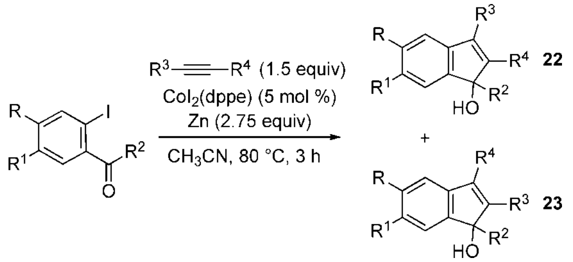
It is noteworthy that it is possible to perform a three-component reaction between *o*-iodobenzaldehyde, *p*-toluidine, and alkynes to form heteroatom-substituted derivatives[67] (Scheme 66).

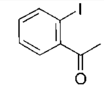
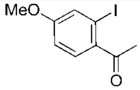
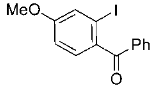
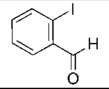
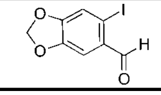
8.2. Cobalt-Catalyzed Heck-Type Reactions

The Heck reaction[68,69] is a powerful tool for the elaboration of carbon−carbon bonds. However, the reaction still suffers some limitations. Thus, the use of alkyl halides having hydrogen(s) atom(s) in the *β*-position to the halide atom leads to poor results, since the intermediate catalytic alkylpalladium species undergoes a very fast *β*-hydrogen elimination. Interestingly, the cobalt-catalyzed Heck type reaction is complementary to the classical palladium-catalyzed reaction, since it allows avoidance of this drawback.

In 1991, Branchaud[70] reported the first cobalt-catalyzed Heck-type reaction between styrene and various alkyl halides (Table 31) in the presence of cobaloxime(II) and a stoichiometric amount of zinc as a reductant. It should be noted that exposure to daylight is necessary.

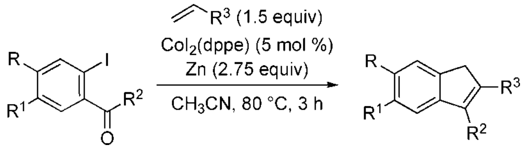
Table 29. Cobalt-Catalyzed Carbocyclization of *ortho*-Iodoaryl Ketones and Aldehydes with Alkynes

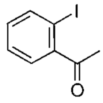
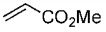
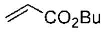
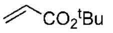
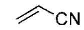
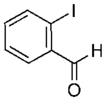
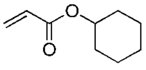


Entry	*o*-Iodoaryl ketone or Aldehyde	R^3	R^4	Yield of **22** (%)
1		Ph	Ph	93
2		Bu	Ph	95 (89/11)[a]
3		TMS	CO$_2$Et	95
4		TMS	CO$_2$Et	70
5		TMS	CO$_2$Et	85
6		Ph	Ph	85
7		Bu	Ph	80 (88/12)[a]
8		TMS	Me	60
9		Ph	Ph	70

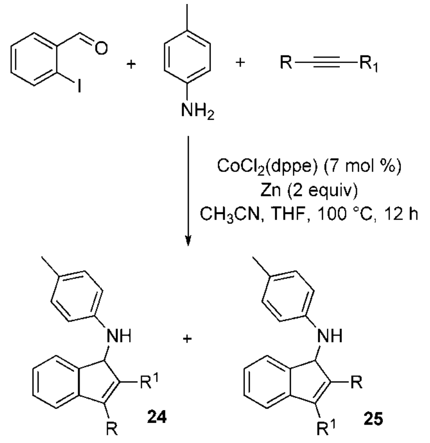
[a] Ratio **22**/**23**.

Table 30. Intermolecular Cyclization of *ortho*-Iodoaryl Ketones and Aldehydes with Acrylic Esters



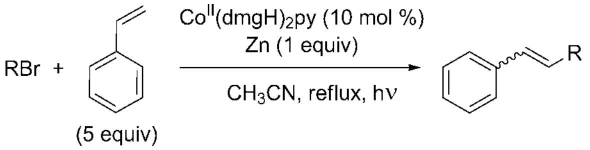
Entry	Starting product	Acrylic Esters	Yield (%)
1			66
2			75
3			41
4			95
5			63
6			62

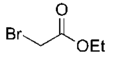
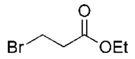
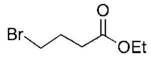
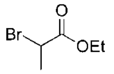
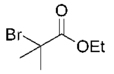
Scheme 66. Cobalt-Catalyzed Three-Component Cyclization Reaction



R= R^1= (CH$_2$)$_2$CH$_3$: 99%
R= R^1= Ph : 78 %
R= CO$_2$Me, R^1= *c*-Hex : 73 % **(25)**
R= Me, R^1= TMS : 95 % **(24)**

Table 31. Cobaloxime-Catalyzed Heck-Type Reaction



Entry	RBr	Yield (%)
1		20
2		45
3		37
4		60
5		0
6	*n*-DecBr	42

Primary (Table 31, entries 1−3 and 6) and secondary (entry 4) alkyl bromides lead to moderate yields whereas the reaction failed with tertiary alkyl bromides (entry 5).

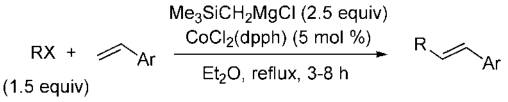
Later, Oshima reported that excellent yields were obtained by using CoCl$_2$•dpph as a catalyst and trimethylsilylmethylmagnesium chloride as a reducing agent (Table 32).[71a]

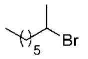
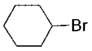
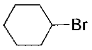
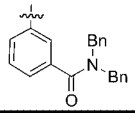
Primary (Table 32, entries 1−3), secondary (entries 4−5 and 8−10), and even tertiary (entry 6) alkyl halides react to give good to excellent yields. As a rule, alkyl bromides afford better yields than the corresponding iodides or chlorides (entries 1−3). Functionalized styrene derivatives can be coupled efficiently (entries 7−10). It is interesting to note that the reaction can be achieved stereoselectively (Scheme 67).

A detailed mechanistic study was performed (Scheme 68).

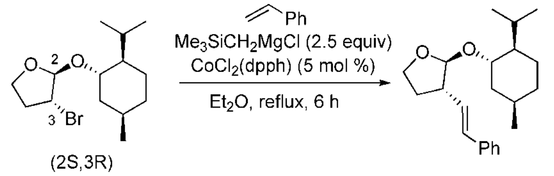
At first, CoCl$_2$•dpph [A] reacts with Me$_3$SiCH$_2$MgCl to give Co^0•dpph [B], which is the real catalyst. A single monoelectronic transfer to the alkyl halide leads to the CoI species [C] that reacts with Me$_3$SiCH$_2$MgCl to give the intermediate [D]. This one reacts with the benzylic radical accruing from RX to produce the diorganocobalt [E]. The Heck product RCH=CHPh is then obtain from [E] by *β*-hydrogen elimination. Finally, Co^0•dpph [B] is regenerated from the hydridocobalt species [F] by reductive elimination.

Table 32. CoCl$_2$(dpph)-Catalyzed Heck-Type Reaction



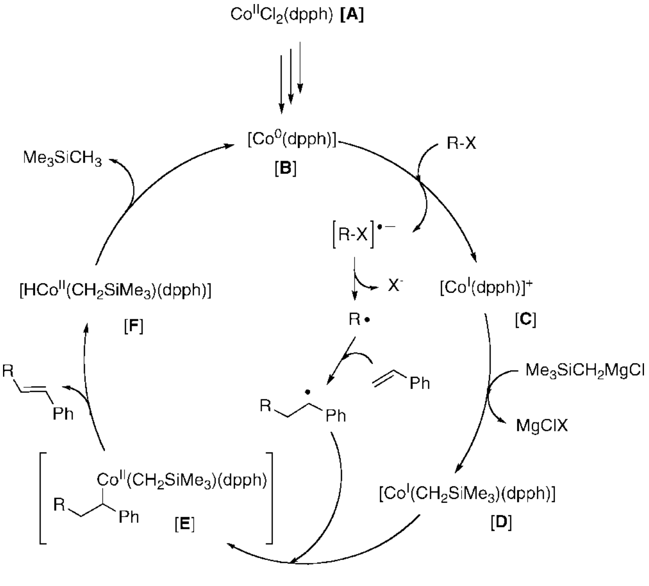
Entry	RX	Ar	Yield (%)
1	n-C12H25I	Ph	57
2	n-C12H25Br	"	76
3	n-C12H25Cl	"	74
4		Ph	73
5		Ph	84
6	t-BuBr	Ph	67
7		p-Cl-C6H4	85
8	"	m-Cl-C6H4	82
9	"	o-Cl-C6H4	85
10	"		95

Scheme 67. Cobalt-Catalyzed Diastereoselective Heck-Type Reaction



68%
(2S,3S)/(2S,3R) > 97:3

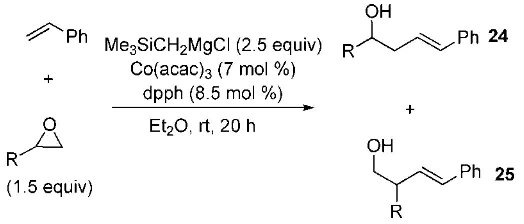
Scheme 68. Mechanism of the CoCl$_2$(dpph)-Catalyzed Heck-Type Reaction



It is important to note that a mechanism involving a Co^I/Co^{III} couple like this one proposed for the vitamin B12- or the cobaloxime-mediated reaction[60,61] cannot be discarded.

The cobalt-catalyzed Heck-type reaction between an epoxide and styrene has also been described (Table 33).[72]

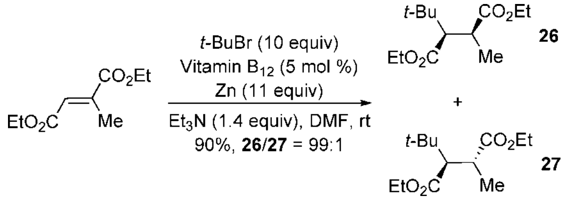
Table 33. Cobalt-Catalyzed Heck-Type Reaction between Epoxides and Styrene



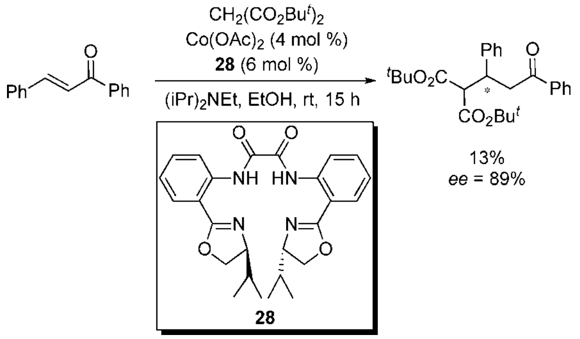
Entry	R	Yield (%)	24/25
1	Me	57	79:21
2	*n*-Bu	58	57:43
3	*c*-C_6H_{11}	48	63:37[a]
4	*t*-Bu	26	>99:1

[a] Toluene is used as solvent.

Scheme 69. Vitamin B12-Catalyzed Michael-like Addition



Scheme 70. Enantioselective Cobalt-Mediated Michael Addition to Chalcone



The reaction leads to moderate yields, and a mixture of isomers is obtained. Thus, except in the case of a hindered epoxide, the stereoselectivity of the reaction is very poor (Table 33, entry 4).

9. Miscellaneous Reactions

9.1. Cobalt-Mediated Michael Addition

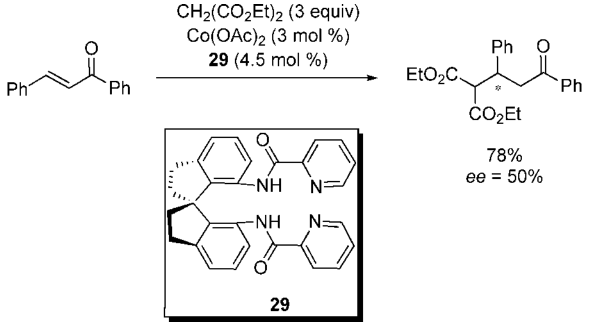
As mentioned above, alkyl and aryl radicals are generated by reacting an alkyl or an aryl halide with various cobalt(II) complexes (see section 8).

Diastereoselective conjugate addition of the radicals thus obtained to activated alkenes has been studied for the first time by Giese[73] in 1992 (Scheme 69). The reaction is performed by using a catalytic amount of vitamin B12 and zinc as a reductant.

In 1998, Pfaltz[74] obtained a poor yield, but a promising high enantiomeric excess, by reacting *tert*-butyl malonate with chalcone in the presence of cobalt acetate and the chiral macroheterocyclic ligand **28** (Scheme 70).

A better yield, but a moderate enantiomeric excess, was obtained by Wu and Zhou[75] by reacting ethyl malonate in the presence of a similar catalytic system (Scheme 71).

Scheme 71. Enantioselective Cobalt-Catalyzed Michael Addition to Chalcone



Scheme 72. Cobalt-Catalyzed Michael Addition to Various Activated Alkenes

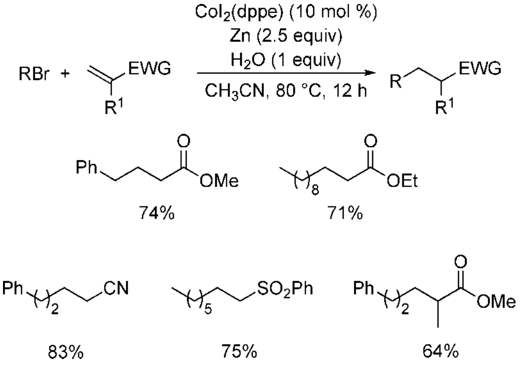
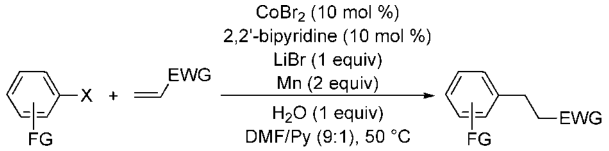


Table 34. Cobalt-Mediated Michael Reaction between Aryl Halides or Triflates and Activated Alkenes



Entry	FG	X	EWG	Yield (%)
1	*p*-CO_2Et	Br	CO_2Et	80
2	*p*-CO_2Et	Br	CN	85
3	*p*-CO_2Et	OTf	CO_2Et	72[a]
4	*p*-CN	Br	CO_2Et	70[a]
5	*p*-CN	Br	CN	77[a]
6	*p*-CN	Cl	CO_2Et	66
7	*p*-CN	OTf	CO_2Et	69[a]

[a] 20 mol % of catalyst was used.

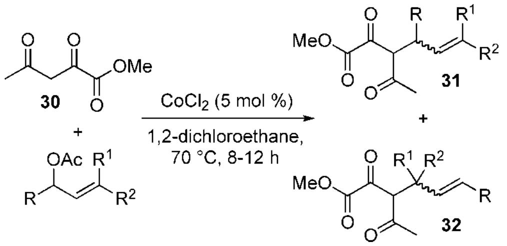
In 2006, a cobalt-mediated Michael addition was performed with alkyl bromides and activated alkenes in the presence of CoI_2(dppe) and zinc as a reductant.[76] Good to excellent yields are obtained (Scheme 72).

Finally, a cobalt-mediated Michael addition from aryl halides or triflates and activated alkenes has also been described by Périchon (Table 34).[77] Aryl bromides (entries 1, 2, 4, and 5), chlorides (entry 6), or triflates (entries 3 and 7) give similar yields. The reaction is chemoselective; thus, ester and cyano groups are tolerated.

9.2. Allylation of 1,3-Dicarbonyl Compounds

The allylation of 1,3-dicarbonyl compounds under cobalt catalysis has been reported by Iqbal.[78] The reaction can be performed under neutral conditions, contrary to the palladium-[79] or the molybdenum-catalyzed[80] reactions. Therefore, the use of base-sensitive substrates like **30** is possible. Selected examples are given in Table 35.

Table 35. Cobalt-Catalyzed Allylation of 1,3-Dicarbonyl Compounds with Allylic Acetates



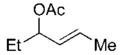
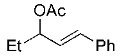
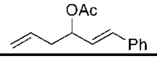
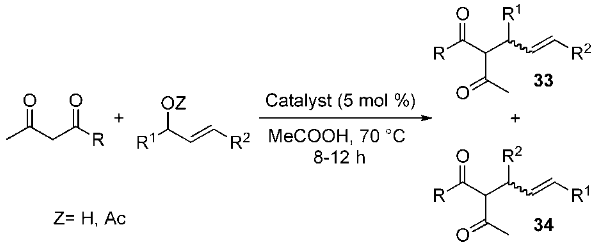
Entry	Allylic Acetate	Yield (%)	**31/32**	E/Z
1		38	20/80	70/30
2		67	90/10	100/0
3		64	70/30	-

Table 36. Cobalt-Catalyzed Allylation of 1,3-Dicarbonyl Compounds with Allylic Alcohol



Entry	Z	R	R^1	R^2	Catalyst	**33/34**	Yield (%)
1	H	Me	Me	Pr	$Co^{III}DMG$	1/8	61
2	Ac	Me	Me	Pr	$CoCl_2$	1/3	68
3	H	OMe	Ph	Et	$Co^{III}DMG$	1/9	64
4	Ac	OMe	Ph	Et	$CoCl_2$	1/3	55
5	H	OMe	Me	Bu	$Co^{III}DMG$	100/0	53
6	Ac	OMe	Me	Bu	$CoCl_2$	1/1.5	24

Moderate to good yields are obtained. Regio- and stereoselectivity heavily depend on the nature of the substrate; a mixture of isomers is often obtained.

This reaction has then been extended to allylic alcohols[81] (Table 36).

9.3. Activation of C−H Bonds: C−N Coupling Reactions

Transition metal-mediated activation and functionalization of C−H bonds is currently a very challenging research area.[82]

Cobalt-porphyrin-catalyzed C−H bond aminations have been widely investigated by Cenini.[83] In 1999, the amination of an allylic C−H bond was described[84a] (Scheme 73).

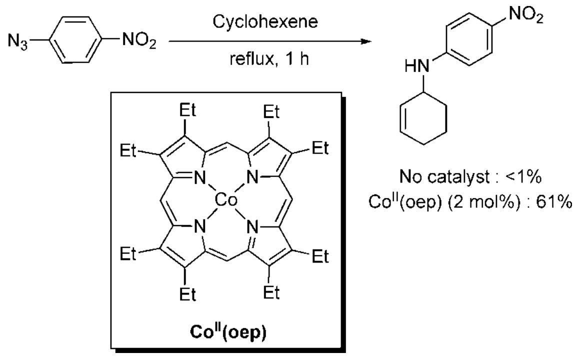
However, only moderate yields are obtained and the scope of the reaction is limited to cyclohexene.

The reaction has then been extended to benzylic C−H bonds.[84b,c] According to the nature of the substrate, an amine or an imine can be obtained in moderate yields (Scheme 74 and Table 37).

9.4. Three-Component Reactions

Multicomponent reactions have emerged as a useful synthetic tool in the past decade.[84] As illustrated above, cobalt salts can be employed as catalysts to achieve such reactions.

Scheme 73. Cobalt-Catalyzed Allylic C−H Bond Amination



Scheme 74. Cobalt-Catalyzed Benzylic C−H Bond Amination

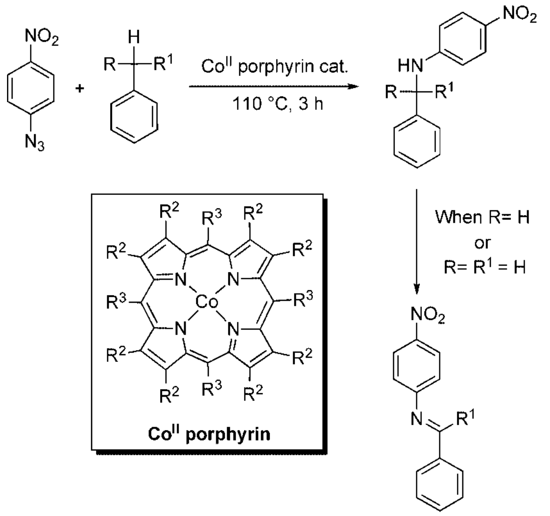


Table 37. Benzylic C−H Amination (see Scheme 74)

Entry	Substrate	Catalyst[a]	Yield (%)	
			Amine	Imine
1	Toluene	A		25
2	Isopropylbenzene	A	53	
3	Cyclohexylbenzene	B	28	
4	Ethylbenzene	A	25	19
5	Diphenylmethane	B	55	11
6	Fluorene	C		41

[a] Co^{II} porphyrin A: $R_2 = H$, $R_3 = p\text{-}Cl{-}C_6H_4$; B: $R_2 = H$, $R_3 = Ph$; C: $R_2 = Et$, $R_3 = H$.

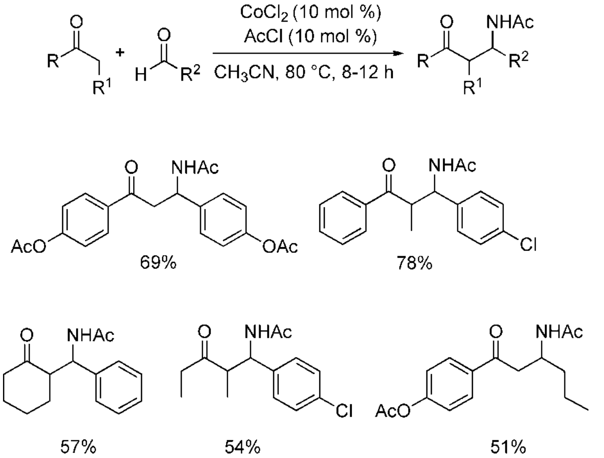
9.4.1. Synthesis of β-Acetamido Ketones

In 1994, Iqbal[85] described a three component reaction between a ketone, an aldehyde, and acetonitrile. Various *β*-acetamido ketones were prepared in moderate to good yields (Scheme 75).

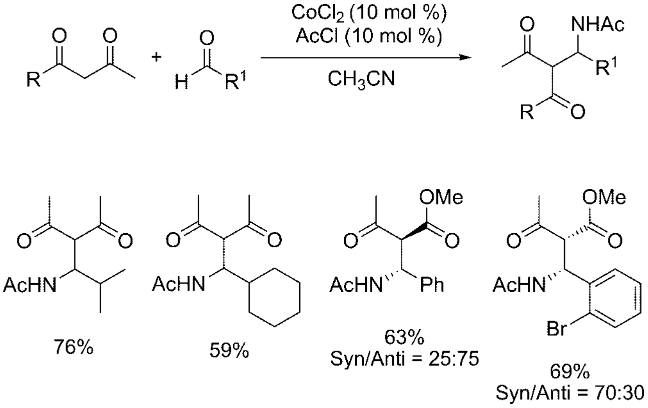
Similarly, the reaction between a 1,3-dicarbonyl compound, an aldehyde, and acetonitrile[86] affords *β*-acetamidodiketones in moderate to good yields (Scheme 76).

It should be noted that aromatic aldehydes lead to acetamidodiketones when the reaction is performed under an inert atmosphere whereas the Knoevenagel adduct is formed in the presence of atmospheric oxygen (Scheme 77). On the other hand, aliphatic aldehydes behave differently, since the acetamidodiketones are obtained only in the presence of atmospheric oxygen. A complex mixture of products is formed when the reaction takes place under an inert atmosphere (Scheme 77).

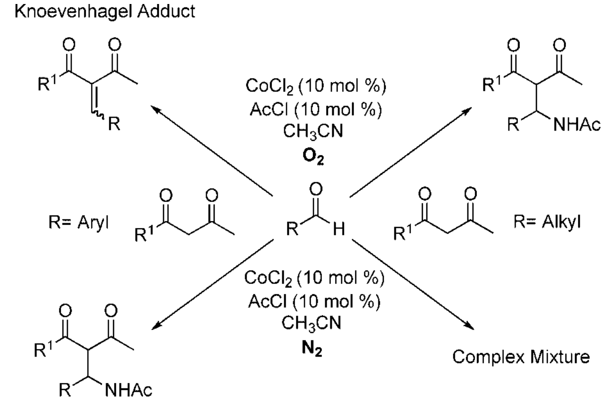
Scheme 75. Synthesis of β-Acetamido Ketones via a Cobalt-Catalyzed Three-Component Reaction



Scheme 76. Synthesis of β-Acetamido Diketones via a Cobalt-Catalyzed Three-Component Reaction



Scheme 77. Cobalt-Catalyzed Reaction between 1,3-Dicarbonyl Compounds, Aldehydes, and Acetonitrile: Influence of the Presence of Oxygen on the Course of the Reaction



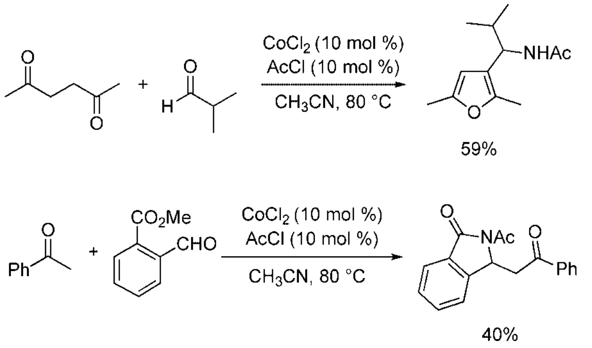
This methodology has been applied to the synthesis of furans and γ-lactams (Scheme 78).

9.4.2. Synthesis of Homoallylsilanes

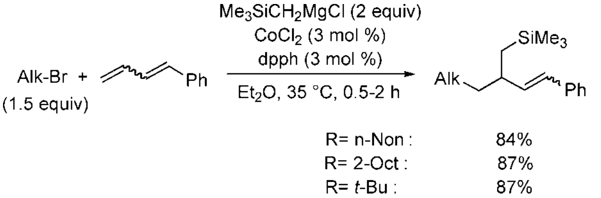
In 2003, Oshima[87] described a cobalt-catalyzed three-component reaction between an alkyl halide, a 1,3-diene, and trimethylsilylmethylmagnesium chloride. Various homoallylsilanes have been synthesized in good to excellent yields from primary, secondary, or tertiary alkyl halides (Scheme 79).

The following catalytic cycle was proposed (Scheme 80).

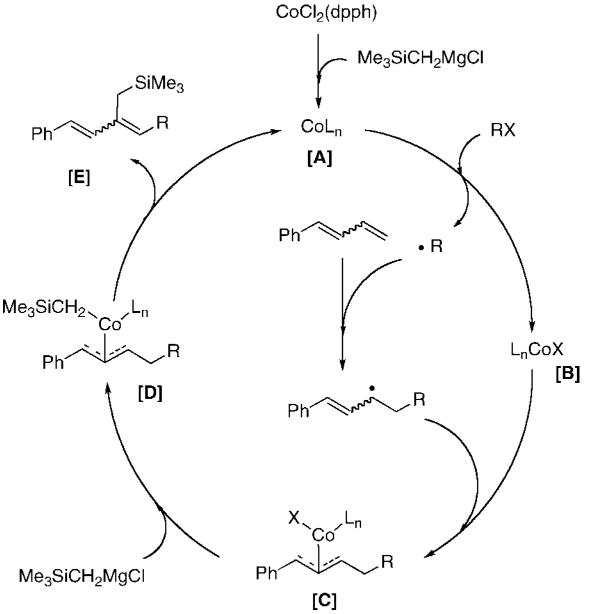
Scheme 78. Synthesis of Furans and γ-Lactams via a Cobalt-Catalyzed Three-Component Reaction



Scheme 79. Synthesis of Homoallylsilanes via a Cobalt-Catalyzed Three-Component Reaction



Scheme 80. Tentative Mechanism for the Formation of Homoallylsilanes via a Cobalt-Catalyzed Three-Component Reaction

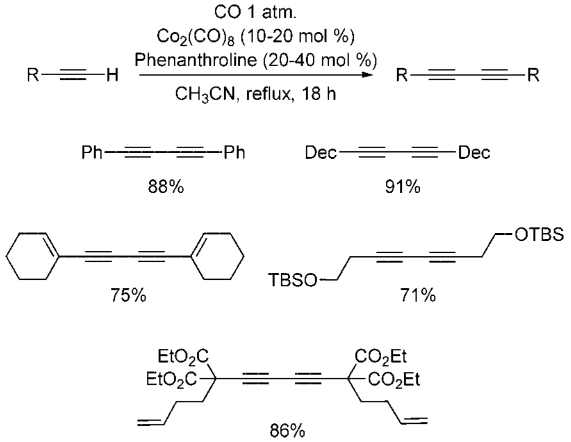


At first, Me_3SiCH_2MgCl reduces cobalt(II) chloride into an active Co^0 species [A]. This one reacts with the alkyl halide via a single electron transfer to form the corresponding alkyl radical and the Co^I complex [B]. Afterward, the alkyl radical adds to the diene to give a new radical, which combines with [B] to form the Co^{II} complex [C]. Me_3SiCH_2MgCl then reacts with [C] to afford the diorganocobalt [D], which undergoes a reductive elimination, leading to the homosilane [E] and to the complex [A].

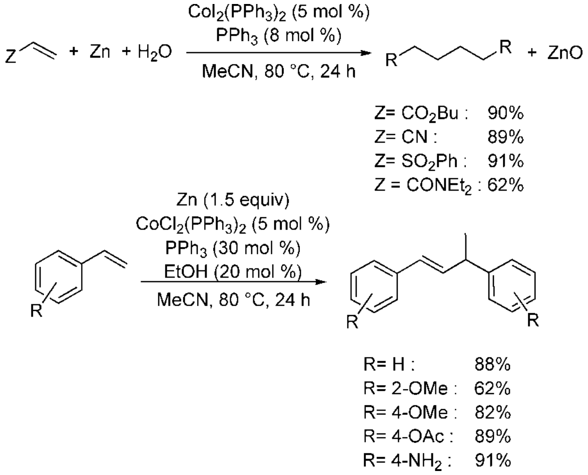
9.5. Coupling of Alkenes and Alkynes

Copper-mediated reactions have been extensively used for the preparation of conjugated diynes.[88] The Glaser[89] and Eglington[90] procedures for the homocoupling of terminal alkynes, or the Cadiot-Chodkiewicz[91] procedure for the

Scheme 81. Cobalt-Catalyzed Dimerization of Terminal Alkynes



Scheme 82. Cobalt-Catalyzed Reductive Dimerization of Activated Alkenes



coupling of a terminal alkyne with a 1-halo-1-alkyne, are probably the most popular coupling reactions for the synthesis of 1,3-diynes. A cobalt-catalyzed reaction can also be used to prepare diynes.[92] Thus, in 2001, Krafft[93] reported the cobalt-catalyzed dimerization of terminal alkynes in excellent yields (Scheme 81). It is noteworthy that, in the case of conjugated enynes, no trace of the Pauson-Khand[94] product is detected.

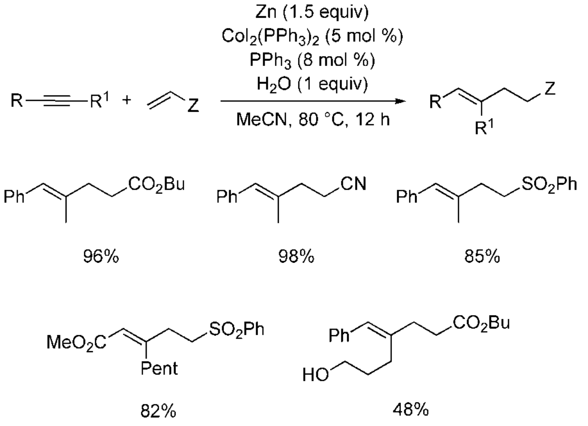
The cobalt-catalyzed reductive dimerization of conjugated alkenes was described by Cheng in 2004.[95] Excellent results are obtained from various activated alkenes or styrenes (Scheme 82). It should be noted that such reactions have been previously performed in the presence of stoichiometric[96] or catalytic[97] amounts of cobalt salts, but the yields are very poor.

The same methodology can be successfully applied to the reductive coupling of internal alkynes with conjugated alkenes.[98] Interestingly, the reaction can be highly regio- and stereoselective. Thus, only one product is obtained from conjugated acetylenic esters and phenylacetylene derivatives (Scheme 83).

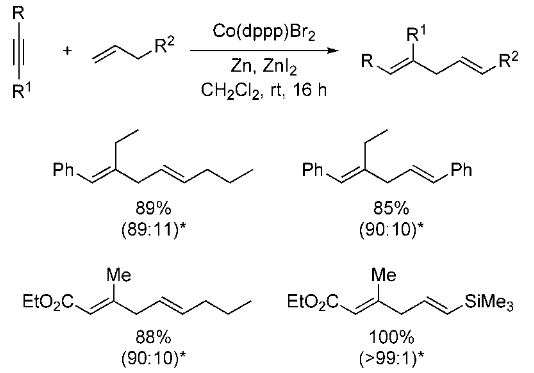
Nonactivated terminal olefins were also used.[99] As a rule, good yields and satisfactory stereoselectivities can be obtained under mild conditions (Scheme 84).

Very recently, Cheng[100] extended the reaction to the intramolecular reductive coupling of activated alkenes with alkynes (Scheme 85). This reaction allows the synthesis of various exomethylenecyclopentane derivatives in good to excellent yields.

Scheme 83. Cobalt-Catalyzed Reductive Coupling of Internal Alkynes with Conjugated Alkenes

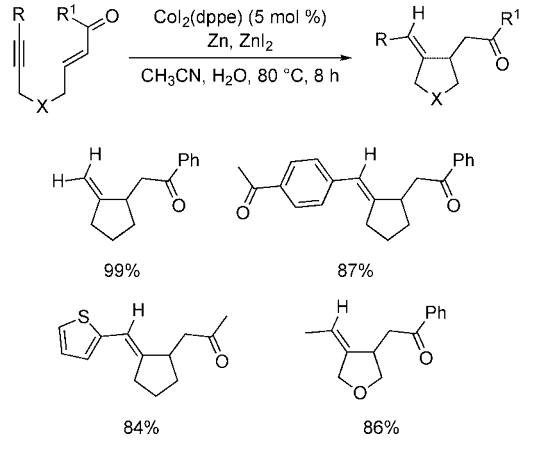


Scheme 84. Cobalt-Catalyzed Alder-Ene Reaction



* *E*/*Z* ratio for the disubstituted double bond.

Scheme 85. Cobalt-Catalyzed Intramolecular Reductive Coupling of Activated Alkenes and Alkynes



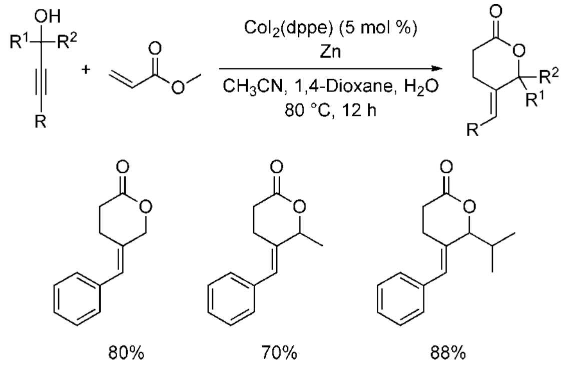
It is noteworthy that it is possible to perform a cobalt-catalyzed intramolecular reductive coupling/lactonization of acrylates with propargyl alcohols (Scheme 86).

When propargyl amine derivatives are used, the reaction leads to the formation of six-membered cyclic lactams (Scheme 87).

9.6. Various Reactions

In 2005, Oshima[101] reported the *syn*-hydrophosphination of alkynes under cobalt catalysis. It should be noted that lanthanide-,[102] palladium-, or nickel-catalyzed[103] reactions

Scheme 86. Cobalt-Catalyzed Intramolecular Reductive Coupling/Lactonization of Acrylates with Propargyl Alcohols



Scheme 87. Cobalt-Catalyzed Intramolecular Reductive Coupling/Lactonization of Acrylates with Propargyl Amines Derivatives

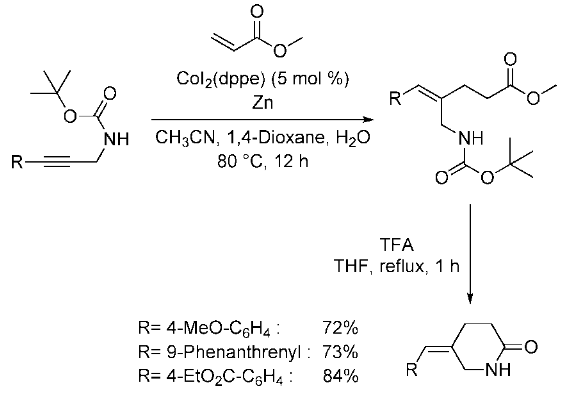
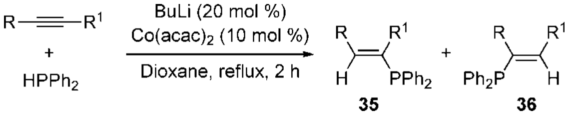


Table 38. Cobalt-Catalyzed *syn*-Hydrophosphination of Alkynes



Entry	R	R¹	Yield (%)	35/36
1	pent	Me	82	66/34
2	Ph	Me	74	82/18
3	*o*-anisyl	Me	41	80/20
4	*t*-Bu	H	81	100/0
5	Ph	H	70	89/11
6	Et_3Si	H	62	94/6

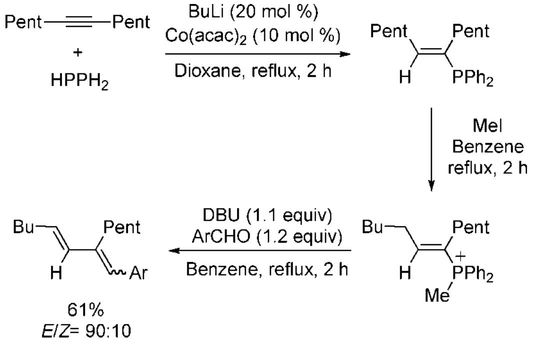
have also been described. However, the stereoselectivity of these reactions is highly dependent on the nature of the substrate. On the contrary, the cobalt-catalyzed reaction mainly leads to the *syn*-addition product **35** (Table 38).

This reaction is of particular interest, since the resulting alkenylphosphine can be used for performing Wittig reactions (Scheme 88).

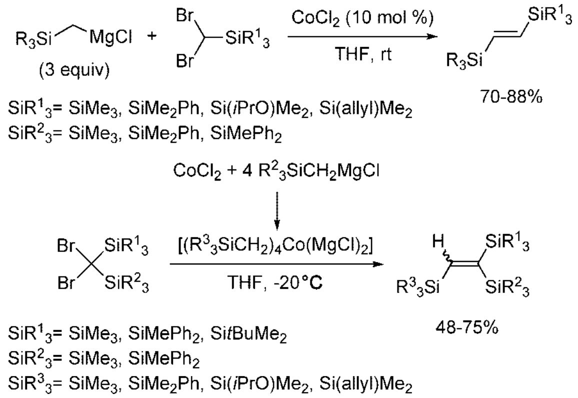
The same year, Oshima[104] reported the preparation of 1,2-di- and 1,1,2-trisilylethylenes via a cobalt-mediated reaction of dibromomethylsilanes with trialkylsilylmethylmagnesium reagents. Disilylethylenes are usually synthesized by hydrosilylation of silylacetylenes[105] or disilylation of acetylenes.[106] Contrary to these reactions, the cobalt-mediated procedure is highly regioselective and stereoselective (Scheme 89).

In 2006, Cheng[107] reported the cobalt-mediated synthesis of thioethers from thiols and aryl halides (Scheme 90). This coupling method is advantageous compared to copper-, palladium-, and nickel-mediated reactions,[108] since mild reaction conditions and low catalyst loading are necessary. Moreover, the use of sophisticated phosphine ligand is avoided.

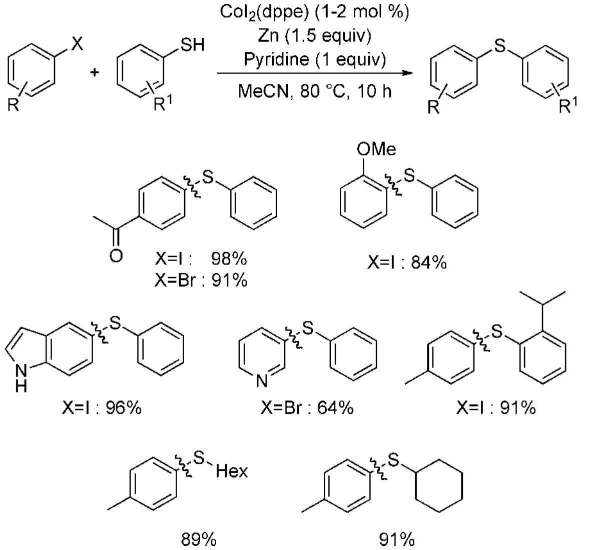
Scheme 88. Cobalt-Catalyzed *syn*-Hydrophosphination of Alkynes: Application to the Wittig Reaction



Scheme 89. Cobalt-Catalyzed Synthesis of 1,2-Di- and 1,1,2-Trisilylethylenes



Scheme 90. Synthesis of Thioethers via Cobalt-Catalyzed C−S Coupling Reaction

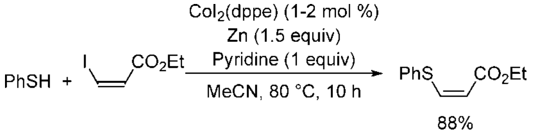


Under these conditions, ethyl 2-iodoacrylate can also be coupled successfully (Scheme 91).

10. Conclusion

Sustainable development prompted organic chemists to look for more ecocompatible and more economical transition metal-catalyzed procedures. Thus, in the last ten years, a growing number of iron- or manganese-catalyzed reactions

Scheme 91. Cobalt-Catalyzed Cross-coupling between Thiophenol and 2-Iodoethyl Acrylate



were proposed to replace the older palladium and nickel-catalyzed cross-coupling procedures. Of course, in the framework of sustainable development, cobalt is less interesting than iron or manganese; however, it compares favorably to nickel and palladium. Thus, cobalt can be an interesting alternative when iron or manganese cannot be used. On the other hand, it should be underlined that several reactions performed under cobalt catalysis are specific to this metal. For instance, iron-catalyzed cross coupling between aryl Grignard reagents and functionalized secondary alkyl bromides generally failed whereas excellent yields are obtained under cobalt catalysis. Thus, in the future, it should be possible to develop more distinct reactions using cobalt-based catalytic systems.

In spite of the numerous interesting reports mentioned in this review, cobalt-catalyzed reactions are still in their infancy. In the future, they should be more extensively developed and could take a significant place in the renewal of transition metal-catalyzed reactions.

11. Acknowledgments

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12. References

(1) Kharasch, M. S.; Fuchs, C. F. *J. Am. Chem. Soc.* **1941**, *63*, 2316.
(2) For reviews, see: (a) Yorimitsu, H.; Oshima, K. *Pure Appl. Chem.* **2006**, *78*, 441. (b) Shinokubo, H.; Oshima, K. *Eur. J. Org. Chem.* **2004**, 2081. (c) Iqbal, J.; Mukhopadhyay, M.; Mandal, A. K. *Synlett* **1997**, 876. (d) Hess, W.; Treutwein, J.; Hilt, G. *Synthesis* **2008**, 3537. (e) Omae, I. *Appl. Organomet. Chem.* **2007**, *21*, 318. (f) Gosmini, C.; Begouin, J.-M.; Moncomble, A. *Chem. Commun.* **2008**, *28*, 3221.
(3) (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc. Perkin Trans. I* **1973**, 977. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Khand, I. U.; Pauson, P. L. *J. Chem. Soc., Chem. Commun.* **1974**, 379. For a review, see: (d) Struebing, D.; Beller, M. *Top. Organomet. Chem.* **2006**, *18*, 165.
(4) (a) Pino, P.; Piacenti, F.; Bianchi, M. In *Organic Synthesis via Metal Carbonyls*; Wender, I., Pino, P., Eds.; Wiley: New York, 1977; Vol. 2, Chapter 2. (b) Pruett, R. L. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1979; Vol. 17, p 1. (c) Paulik, F. E. *Catal. Rev.* **1972**, *6*, 49. (d) Orchin, M.; Replius, W. *Catal. Rev.* **1972**, *6*, 85. (e) Heck, R. F.; Breslow, D. S. *J. Am. Chem. Soc.* **1961**, *83*, 4023. (f) Mirback, M. F. *J. Organomet. Chem.* **1984**, *265*, 205. (g) Klinger, R. J.; Rathke, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 4772. (h) Ojima, I.; Tsai, C.-Y.; Tzamarioudaki, M.; Bonafoux, D. *Org. React.* **2000**, *56*, 1. (i) Wiese, K.-D.; Obst, D. *Top. Organomet. Chem.* **2006**, *18*, 1.
(5) Leading references: (a) Zhu, S.; Ruppel, J. V.; Lu, H.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042. (b) Penoni, A.; Wanke, R.; Tollari, S.; Gallo, E.; Musella, D.; Ragaini, F.; Demartin, F.; Cenini, S. *Eur. J. Inorg. Chem.* **2003**, 1452. (c) Ikeno, T.; Iwakura, I.; Yabushita, S.; Yamada, T. *Org. Lett.* **2002**, *4*, 517. (d) Uchida, T.; Saha, B.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 2521. (e) Kanai, H.; Matsuda, H. *J. Mol. Catal.* **1985**, *29*, 157. (f) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3443. (g) Fantauzzi, S.; Gallo, E.; Rose, E.; Raoul, N.; Caselli, A.; Issa, S.; Ragaini, F.; Cenini, S. *Organometallics* **2008**, *27*, 6143, and references cited therein.
(6) (a) Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1984**, *23*, 539. (b) Grotjahn, D. B.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 2091. (c) Butenschon, H.; Winkler, M.; Vollhardt, K. P. C. *Chem. Commun.* **1986**, 388. (d) Johnson, E. P.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1991**, *113*, 381. For reviews, see: (e) Wu, M. S.; Shanmugansundaram, M.; Cheng, C.-H. *Chem. Commun.* **2003**, 718. (f) Aubert, C.; Buisine, O.; Petit, M.; Slowinski, F.; Malacria, M. *Pure Appl. Chem.* **1999**, *71*, 1463. (g) Bonãga, L. V. R.; Zhang, H.-C.; Moretto, A. F.; Ye, H.; Gauthier, D. A.; Li, J.; Leo, G. C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2005**, *127*, 3473. (h) Agenet, N.; Gandon, V.; Vollhardt, K. P. C.; Malacria, M.; Aubertand, C. *J. Am. Chem. Soc.* **2007**, *129*, 8860. (i) Scheuermann née Taylor, C. J.; Ward, B. D. *New J. Chem.* **2008**, *32*, 1850. For a recent communication, see: (j) Geny, A.; Agenet, N.; Iannazzo, L.; Malacria, M.; Aubert, C.; Gandon, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 1810, and references cited therein.
(7) Chen, K. C.; Rayabarapu, D. K.; Wang, C. C.; Cheng, C.-H. *J. Org. Chem.* **2001**, *66*, 8804, and references cited therein.
(8) Gilman, H.; Lichtenwalter, M. *J. Am. Chem. Soc.* **1939**, *61*, 957.
(9) (a) Morizur, J. P.; Pallaud, R. C. R. *Acad. Sci. Paris* **1962**, *254*, 1093. (b) Morizur, J. P. *Bull. Soc. Chim. Fr.* **1964**, 1331.
(10) Kharasch, M. S.; Fuchs, C. F. *J. Am. Chem. Soc.* **1943**, *65*, 504.
(11) (a) Uemura, S.; Fukuzawa, S.-I. *Tetrahedron Lett.* **1982**, *23*, 1181. (b) Uemura, S.; Fukuzawa, S.-I.; Path, S. R. *J. Organomet. Chem.* **1983**, *243*, 9.
(12) (a) Cahiez, G.; Avedissian, H. *Tetrahedron Lett.* **1998**, *39*, 6159. The beneficial influence of NMP on iron-catalyzed alkenylation reactions was also described: (b) Cahiez, G.; Marquais, S. *Tetrahedron Lett.* **1996**, *37*, 1773. (c) Cahiez, G.; Marquais, S. *Pure Appl. Chem.* **1996**, *68*, 53. (d) Cahiez, G.; Avedissian, H. *Synthesis* **1998**, 1199. NMP has also a favorable effect on the Cu-catalyzed alkylation of organomagnesium and organomanganese halides. (e) Cahiez, G.; Marquais, S. *Synlett* **1993**, 45. See also ref.[12c]
(13) Shirakawa, E.; Imazaki, Y.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 654.
(14) Amatore, M.; Gosmini, C.; Périchon, J. *Eur. J. Org. Chem.* **2005**, 989.
(15) Buriez, O.; Nédélec, J.-Y.; Périchon, J. *J. Electroanal. Chem.* **2001**, *506*, 162.
(16) (a) Korn, T. J.; Cahiez, G.; Knochel, P. *Synlett* **2003**, *12*, 1892. (b) Ohmiya, H.; Yorimitu, H.; Oshima, K. *Chem. Lett.* **2004**, *33*, 1240.
(17) Hatakeyama, T.; Hashimoto, S.; Ishizuka, K.; Nakamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 11949.
(18) Korn, T. J.; Knochel, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 2947.
(19) 4-Fluorostyrene has already been used as an additive to perform cross-coupling reactions:Jensen, A. E.; Knochel, P. *J. Org. Chem.* **1988**, *53*, 2390. See also: Johnson, J. B.; Rovis, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 840.
(20) (a) Korn, T.; Schade, M.; Schade, S.; Knochel, P. *Org. Lett.* **2006**, *8*, 725. (b) Korn, T. J.; Schade, M. A.; Cheemala, M. N.; Wirth, S.; Guevara, S. A.; Cahiez, G.; Knochel, P. *Synthesis* **2006**, 3547.
(21) For the use of aryl fluorides, see: (a) Cahiez, G.; Lepifre, F.; Ramiandrasoa, P. *Synthesis* **1999**, 2138. (b) Dankwardt, J. W. J. *Organomet. Chem.* **2005**, *690*, 932, and references cited therein. (c) Bahmanyar, S.; Borer, B. C.; Kim, Y. M.; Kurtz, D. M.; Yu, S. *Org. Lett.* **2005**, *7*, 1011. (d) Saeki, T.; Takashima, Y.; Tamao, K. *Synlett* **2005**, 1771. (e) Ackermann, L.; Born, R.; Spatz, J. H.; Meyer, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 7216.
(22) For the use of aryl tosylates, see: (a) Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222. (b) Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3910. (c) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653. (d) Tang, Z.-Y.; Hu, Q.-S. *J. Am. Chem. Soc.* **2004**, *126*, 3058, and references cited therein. (e) Limmert, M. E.; Roy, A. H.; Hartwig, J. F. *J. Org. Chem.* **2005**, *70*, 9364, and references cited therein.
(23) (a) Amatore, M.; Gosmini, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2089. Very recently, Gosmini also described the formation of symmetrical biaryls under similar conditions. See: (b) Moncomble, A.; Le Floch, P.; Gosmini, C. *Chem.—Eur. J.* **2009**, *15*, 4770.
(24) Kharasch, M. S.; Fuchs, C. F. *J. Am. Chem. Soc.* **1945**, *10*, 292.
(25) Cahiez, G.; Avedisssian, H. Unpublished results.
(26) Avedissian, H.; Bérillon, L.; Cahiez, G.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 6163.
(27) Kamachi, T.; Kuno, A.; Matsuno, C.; Okamoto, S. *Tetrahedron Lett.* **2004**, *45*, 4677.
(28) Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Inamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128*, 8068.
(29) Tsuji, T.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 1886.
(30) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2006**, *8*, 3093.
(31) Davies, D. I.; Done, J. N.; Hey, D. H. *J. Chem. Soc. C* **1969**, 2019.

(32) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374.
(33) Someya, H.; Kondoh, A.; Sato, A.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Synlett* **2006**, *18*, 3061.
(34) (a) Tamao, K.; Nakajima, T.; Kumada, M. *Organometallics* **1984**, *3*, 1655. (b) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29.
(35) Ohmiya, H.; Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 2207.
(36) Kobayashi, Y.; Nakata, K.; Ainai, T. *Org. Lett.* **2005**, *7*, 183.
(37) Cahiez, G.; Chaboche, C.; Duplais, C.; Moyeux, A. *Org. Lett.* **2009**, *11*, 277.
(38) Hamaguchi, H.; Uemura, M.; Yasui, H.; Yorimitsu, H.; Oshima, K. *Chem. Lett.* **2008**, *37*, 1178.
(39) Gomes, P.; Gosmini, C.; Périchon, J. *Org. Lett.* **2003**, *5*, 1043.
(40) (a) Durandetti, M.; Nédélec, J.-Y.; Périchon, J. *J. Org. Chem.* **1996**, *61*, 1748. (b) Gomes, P.; Gosmini, C.; Périchon, J. *J. Org. Chem.* **2003**, *68*, 1142. (c) Gomes, P.; Gosmini, C.; Périchon, J. Fr. Pat. Appl. 01/08808, July 3, 2001.
(41) (a) Mizutani, K.; Yorimitsu, H.; Oshima, K. *Chem. Lett.* **2004**, *33*, 832. (b) Yasui, H.; Mizutani, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 1410.
(42) Kharasch, M. S.; Lambert, F. L.; Urry, W. H. *J. Org. Chem.* **1945**, *10*, 298.
(43) Schlubach, H. H.; Franzen, V. I. *Liebigs Ann. Chem.* **1951**, *572*, 116.
(44) Black, H. K.; Horn, D. H. S.; Weedon, B. C. L. *J. Chem. Soc. C* **1954**, 1704.
(45) Kuno, A.; Saino, N.; Kamachi, T.; Okamoto, S. *Tetrahedron Lett.* **2006**, *47*, 2591.
(46) Someya, H.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 1565.
(47) Shirakawa, E.; Sato, T.; Imazaki, Y.; Kimura, T.; Hayashi, T. *Chem. Commun.* **2007**, 4513.
(48) Reddy, C. K.; Knochel, P. *Angew. Chem., Int. Ed.* **1996**, *35*, 1700.
(49) (a) Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 21. (b) Ohmiya, H.; Tsuji, T.; Yorimitsu, H.; Oshima, K. *Chem.—Eur. J.* **2004**, *10*, 5640.
(50) Cahiez, G.; Chaboche, C.; Giulliani, A.; Duplais, C.; Moyeux, A. *Adv. Synth. Catal.* **2008**, *350*, 1484.
(51) Kharasch, M. S.; Morrison, R.; Urry, W. H. *J. Am. Chem. Soc.* **1944**, *66*, 368.
(52) (a) Kazmierski, I.; Bastienne, M.; Gosmini, C.; Paris, J.-M.; Périchon, J. *J. Org. Chem.* **2004**, *69*, 936. A similar reaction has been previously reported from arylzinc halides prepared *via* an electrochemical procedure. (b) Fillon, H.; Gosmini, C.; Périchon, J. *Tetrahedron* **2003**, *59*, 8199.
(53) For a general review of transition metal-promoted free-radical reactions in organic synthesis, see: Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
(54) For reviews on cobalt-mediated radical reactions in organic synthesis, see: (a) Bhandal, H.; Patel, V. F.; Pattenden, G.; Russel, J. J. *J. Chem. Soc., Perkin Trans. I* **1990**, 2691. (b) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361.
(55) Tiecco, M. *Chem. Commun.* **1965**, 555.
(56) (a) Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775. (b) Okabe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 5382.
(57) Last, K.; Hoffmann, H. M. R. *Synthesis* **1989**, 901.
(58) (a) Ladlow, M.; Pattenden, G. *Tetrahedron Lett.* **1984**, *25*, 4317. (b) Bhandhal, H.; Pattenden, G.; Russel, J. J. *Tetrahedron Lett.* **1986**, *27*, 2299. (c) Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. I* **1988**, 1095.
(59) For a review on the use of Vitamin B_{12} as a catalyst, see: Schrauzer, G. N. *Angew. Chem., Int. Ed.* **1976**, *15*, 417.
(60) Clark, A. J.; Jones, K. *Tetrahedron Lett.* **1989**, *30*, 1989.
(61) Giese, B.; Erdmann, P.; Göbel, T.; Springer, R. *Tetrahedron Lett.* **1989**, *30*, 1989.
(62) (a) Clark, A. J.; Davies, D. I.; Jones, K. J.; Millbanks, C. *J. Chem. Soc., Chem. Commun.* **1994**, 41. A single example of a similar reaction has been described by Knochel: (b) Kneisel, F. F.; Monguchi, Y.; Knapp, K. M.; Zipse, H.; Knochel, P. *Tetrahedron Lett.* **2002**, *43*, 4875.
(63) Fujioka, T.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2002**, *4*, 2257.
(64) (a) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. *Org. Lett.* **2003**, *5*, 3963. (b) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. *J. Org. Chem.* **2004**, *69*, 4781.
(65) (a) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3545. (b) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 9485. (c) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. J. *Tetrahedron Lett.* **1999**, *40*, 4089.
(66) (a) Rayabarapu, D. K.; Cheng, C.-H. *Chem. Commun.* **2002**, 942. (b) Rayabarapu, D. K.; Yang, C.-H.; Cheng, C.-H. *J. Org. Chem.* **2003**, *68*, 6726.
(67) Liu, C.-C.; Korivi, R. P.; Cheng, C.-C. *Chem.—Eur. J.* **2008**, *14*, 9503.
(68) (a) Mizorocki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320.
(69) For reviews see: (a) Bräse, S.; De Meijere, A. In *Metal Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; Chapter 3. (b) Link, J. T.; Overman, L. E. In *Metal Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; Chapter 6. (c) Bräse, S.; De Meijere, A. In *Metal Catalyzed Cross-Coupling Reactions*, 2nd ed.; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 2004; Chapter 5. (d) Heck, R. F. *Org. React.* **1982**, *27*, 345. (e) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (f) Crips, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (g) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed.* **1994**, *33*, 2379. (h) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (i) Beller, M.; Riermeier, T. H.; Stark, G. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 1, Chapter 2.13. (j) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, 2002; Vol. 1, Chapter IV.2.
(70) Branchaud, B. P.; Detlefsen, W. D. *Tetrahedron Lett.* **1991**, *32*, 6273.
(71) (a) Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 6514. (b) Recently, Bao reported that a Heck-type reaction can be performed in the presence of cobalt nanospheres: Zhou, P.; Li, Y.; Sun, P.; Zhou, J.; Bao, J. *Chem. Commun.* **2007**, 1418.
(72) Ikeda, Y.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Adv. Synth. Catal.* **2004**, *346*, 1631.
(73) Erdmann, P.; Schäfer, J.; Springer, R.; Zeitz, H.-G.; Giese, B. *Helv. Chim. Acta* **1992**, *75*, 638.
(74) End, N.; Macko, L.; Zehnder, M.; Pfaltz, A. *Chem.—Eur. J.* **1998**, *4*, 818.
(75) Chen, C.; Zhu, S.-F.; Wu, X.-Y.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2006**, *17*, 2761.
(76) Shukla, P.; Hsu, Y.-C.; Cheng, C.-H. *J. Org. Chem.* **2006**, *71*, 655.
(77) Amatore, M.; Gosmini, C.; Périchon, J. *J. Org. Chem.* **2006**, *71*, 6130.
(78) (a) Bhatia, B.; Reddy, M. M.; Iqbal, J. *Tetrahedron Lett.* **1993**, *34*, 6301. (b) Maikap, G. C.; Reddy, M. M.; Mukhopadhyay, M.; Bhatia, B.; Iqbal, J. *Tetrahedron* **1994**, *50*, 9145.
(79) (a) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. (b) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (c) Heck, R. F. *Palladium reagents in organic synthesis*; Academic Press: London, 1985. (d) Godleski, S. A. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, 1991; Vol. 4, p 585.
(80) (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1992**, *104*, 5543. (b) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1983**, *105*, 3343. (c) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.
(81) Mukhopadhyay, M.; Iqbal, J. *Tetrahedron Lett.* **1995**, *36*, 6761.
(82) For a review on C−H activation by metal complexes, see: Shilov, A. E.; Shul'pin, G. B. Chem. Rev. 1997, *97*, 2879.
(83) (a) Cenini, S.; Tollari, S.; Penoni, A.; Cereda, C. *J. Mol. Catal. A* **1999**, 135. (b) Cenini, S.; Gallo, E.; Penoni, A.; Ragaini, F.; Tollari, S. *Chem. Commun.* **2000**, 2265. (c) Ragaini, F.; Penoni, A.; Gallo, E.; Tollari, S.; Li Gotti, C.; Lapadula, M.; Mangioni, E.; Cenini, S. *Chem.—Eur. J.* **2003**, *9*, 249.
(84) For reviews, see: (a) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168. (b) Terret, N. K.; Gardner, M.; Gordon, D. W.; Kobylecki, R. J.; Steele, J. *Tetrahedron* **1995**, *51*, 8135. (c) Thomson, L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555. (d) Ellman, J. A. *Acc. Chem. Res.* **1996**, *29*, 132.
(85) (a) Bhatia, B.; Reddy, M. M.; Iqbal, J. *J. Chem. Soc., Chem. Commun.* **1994**, 713. (b) Mukhopadhyay, M.; Bhatia, B.; Iqbal, J. *Tetrahedron Lett.* **1997**, *38*, 1083.
(86) (a) Reddy, M. M.; Bhatia, B.; Iqbal, J. *Tetrahedron Lett.* **1995**, *36*, 4877. (b) Nageshwar Rao, I.; Prabhakaran, E. N.; Das, S. K.; Iqbal, J. *J. Org. Chem.* **2003**, *68*, 4079. (c) This reaction can be achieved using a polyaniline-supported cobalt catalyst: Prabhakaran, E. N.; Iqbal, J. *J. Org. Chem.* **1999**, *64*, 3339.
(87) Mizutani, K.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2003**, *5*, 3959.
(88) (a) For a comprehensive review on alkynyl−alkynyl coupling, see: Siemsen, P.; Livngston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632. (b) For a general review on coupling reactions between *sp*-carbon centers, see: Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 3, p 551.
(89) (a) Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320. (b) Nicolaou, K. C.; Petasis, N. A.; Zipkin, R. E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555. For a recent publication, see, for example: (c) Hilt, G.; Hengst, C.; Arndt, M. *Synthesis* **2009**, 395.
(90) (a) Berscheid, R.; Vögtle, F. *Synthesis* **1992**, 58. (b) Nicolaou, K. C.; Zipkin, R. E.; Petasis, N. A. *J. Am. Chem. Soc.* **1982**, *104*, 5558. (c) Nomoto, T.; Fukui, K.; Nakagawa, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 305. (d) Eglington, G.; Galbraith, A. R. *J. Chem. Soc.* **1959**, 889.

(91) (a) Ando, T.; Vu, M. H.; Yoshida, S.; Takahashi, N. *Agric. Biol. Chem.* **1982**, *46*, 717. (b) Crombie, L.; Hobbs, A. J. W.; Horsham, M. A. *Tetrahedron Lett.* **1987**, *28*, 4875. (c) Miller, J. A.; Zweifel, G. *Synthesis* **1983**, 128.

(92) For a review, see: Jeganmohan, M.; Cheng, C.-C. *Chem.—Eur. J.* **2008**, *14*, 10876.

(93) Krafft, M. E.; Hirosawa, C.; Dalal, N.; Ramsey, C.; Stiegman, A. *Tetrahedron Lett.* **2001**, *42*, 7733.

(94) Dicobalt octacarbonyl is known to be an efficient catalyst for the Pauson-Khand reaction; for instance, see: Krafft, M. E.; Bonãga, L. V.; Hirosawa, C. *J. Org. Chem.* **2001**, *66*, 3004, and references cited therein.

(95) Wang, C.-C.; Lin, P.-S.; Cheng, C.-H. *Tetrahedron Lett.* **2004**, *45*, 6203.

(96) Agnès, G.; Chiusoli, G. P.; Cometti, G. *Chem. Commun.* **1968**, 1515.

(97) (a) Kanai, H.; Okada, M. *Chem. Lett.* **1975**, 167. (b) Kanai, H.; Ishii, K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1015.

(98) Wang, C.-C.; Lin, P.-S.; Cheng, C.-H. *J. Am. Chem. Soc.* **2002**, *124*, 9696.

(99) Hilt, G.; Treutwein, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8500.

(100) Chang, H.-T.; Jayanth, T. T.; Wang, C.-C.; Cheng, C.-C. *J. Am. Chem. Soc.* **2007**, *129*, 12032.

(101) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 2368.

(102) (a) Douglass, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 1824. (b) Douglass, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10221. (c) Kawaoka, A. M.; Douglass, M. R.; Marks, T. J. *Organometallics* **2003**, *22*, 4630. (d) Takaki, K.; Takeda, M.; Koshoji, G.; Shishido, T.; Takehira, K. *Tetrahedron Lett.* **2001**, *42*, 6357. (e) Takaki, K.; Koshoji, G.; Komeyama, K.; Takeda, M.; Shishido, T.; Kitani, A.; Takehira, K. *J. Org. Chem.* **2003**, *68*, 6554. (f) Takaki, K.; Komeyama, K.; Takehira, K. *Tetrahedron* **2003**, *59*, 10381.

(103) For the addition of phosphane-borane to alkynes under palladium catalysis, see: (a) Mimeau, D.; Gaumont, A.-C. *J. Org. Chem.* **2003**, *68*, 7016. For the transition metal-catalyzed addition of tertiary phosphines to alkynes, see: (b) Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2000**, *122*, 2387.

(104) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 3488.

(105) (a) Suzuki, T.; Lo, P. Y. *J. Organomet. Chem.* **1990**, *391*, 19. (b) Lukevics, E.; Belyakova, Z. V.; Pomerantseva, M. G.; Voronkov, M. G. *J. Organomet. Chem. Libr.* **1977**, *5*, 1. (c) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; p 1479. (d) *Comprehensive Handbook on Hydrosilylation*; Marciniec, B., Ed.; Pergamon: Oxford, 1992. (e) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 8, Chapter 3.12. (f) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317.

(106) (a) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (b) Hibino, J.; Nakatsukasa, S.; Fugami, K.; Matsubara, S.; Oshima, K.; Nozaki, H. *J. Am. Chem. Soc.* **1985**, *107*, 6416. (c) Watanabe, H.; Kobayashi, M.; Saito, M.; Nagai, Y. *J. Organomet. Chem.* **1981**, *216*, 149.

(107) Wong, Y.-C.; Jayanth, T. T.; Cheng, C.-H. *Org. Lett.* **2006**, *8*, 5613.

(108) For the Cu-catalyzed coupling of aryl halides with thiols, see: (a) Bates, C. G.; Gujadhur, R. K.; Venkatamaran, D. *Org. Lett.* **2002**, *4*, 2803. (b) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517. (c) Wu, Y.-J.; He, H. *Synlett* **2003**, 1789. (d) Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkatamaran, D. *Org. Lett.* **2004**, *6*, 5005. (e) Deng, W.; Zou, Y.; Wang, Y.-F.; Liu, L.; Guo, Q.-X. *Synlett* **2004**, 1254. For Pd-catalyzed reactions, see: (f) Mispelaere-Canivet, C.; Spindler, J.-F.; Perrio, S.; Beslin, P. *Tetrahedron* **2005**, *61*, 5253. (g) Itoh, T.; Mase, T. *Org. Lett.* **2004**, *6*, 4587. (h) Fernàndez Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 2180. (i) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397. (j) Schopfer, U.; Schlapbach, A. *Tetrahedron* **2001**, *57*, 3069. (k) Li, G. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513. For Ni-catalyzed reactions, see: (l) Cristau, H. J.; Chabaud, B.; Chêne, A.; Christol, H. *Synthesis* **1981**, 892. (m) Millois, C.; Diaz, P. *Org. Lett.* **2000**, *2*, 1705. (n) Percec, V.; Bae, J. Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 6895. (o) Takagi, K. *Chem. Lett.* **1987**, 2221.

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