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Transformations of Chloroarenes, Catalyzed by Transition-Metal Complexes

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Contents

I. Introduction

Aromatic halides (ArX) are of genuine importance in synthetic organic chemistry. However, applications of haloarenes for synthesis are rather limited due to the inertness of their C–X bonds. Unlike alkyl halides, haloarenes exhibit low reactivity toward nucleophiles even under drastic conditions, unless the carbon–halogen bond is activated by strong electron-withdrawing substituents on the aromatic ring.[1] Enhancement of the poor reactivity of aryl halides is one of the most challenging problems and desirable goals in modern synthetic chemistry. If haloarenes could be used for facile introduction of the aromatic moiety to various organic compounds, this might lead to revolutionary changes in manufacturing of many valuable aromatic products for industrial needs. Polyfunctional derivatives of benzene, naphthalene, and a number of aromatic heterocycles are of special value for the production of polymers, medicines, dyes, explosives, and chemicals for agriculture. It is not surprising, therefore, that attention of numerous research groups has been focused for many years on activation, cleavage, and functionalization of the carbon–halogen bond in aryl halides. This effort was not in vain, as several interesting and promising processes have been developed for utilization of haloarenes in synthesis. Ullmann-type reactions[2] and aromatic substitution, via an $S_{RN}1$ mechanism,[3] represent two of the most impressive examples. However, most arylations with aryl halides employ bromo- and iodoarenes which exhibit much higher reactivity than their chloro and fluoro analogues. The order of reactivity, ArI > ArBr > ArCl > ArF, is consistent with the strength of the Ar–X bond. For instance, the experimentally found bond dissociation energies for phenyl halides (D_{Ph-X}) are 126, 96, 81, and 65, kcal/mol at 298 K for X = F, Cl, Br, and I, respectively.[4,5]

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Unfortunately, the most reactive iodo- and bromoarenes are the most expensive ones, whereas aryl fluorides are both costly and unreactive. Chloroarenes are certainly the most attractive aryl halides for synthetic applications on an industrial scale, because they are inexpensive and readily available in bulk quantities. The main drawback here is the exceedingly high stability of the aromatic carbon–chlorine bond whose inertness remains the major obstacle on the way to wide utilization of chloroarenes. How can the C–Cl bond in aryl chlorides be activated, cleaved, and functionalized? Some significant examples follow.

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(1) Introduction of strong electron-withdrawing groups, such as NO_2, to the ortho and/or para positions of chlorobenzene makes the substrate susceptible to S_NAr-type reactions.[1] This is probably the oldest approach to the aromatic C–Cl bond activation. However, the presence of nitro groups on the aromatic ring is undesirable in many cases, and the problem of their removal thus arises. In order to remove the nitro group, a multistep procedure is applied, involving hydrogenation to the corresponding amine, its diazotization, and reduction of the diazonium cation. The reaction sequence is far from ideal with respect to the overall yield. In addition, not many functional groups can survive during all these transformations.

(2) The aromatic carbon–chlorine bond can be activated under $S_{RN}1$-type reaction conditions.[3] Unfortunately, the number of such reactions involving chloroarenes is very limited, in contrast with the rich $S_{RN}1$ chemistry of iodo- and bromoarenes.

(3) Deprotonation at one of the positions ortho to the chlorine, followed by elimination of the Cl^-, results in the formation of benzyne, which possesses very high reactivity and can be used for the synthesis of various valuable compounds. However, deprotonation of chloroarenes by ordinary bases requires quite drastic conditions. Besides that, the addition of nucleophiles to arynes often leads to mixtures of isomers as the nucleophile can attack at one or other of the sp-carbons.[6]

(4) Chloro derivatives of aromatic[7] and pseudoaromatic[8] compounds can be easily converted to the corresponding chloronium ions, $[ArClAr']^+$, which readily and smoothly react with even weak nucleophiles under exceedingly mild conditions.[7,8] Although aromatic chloronium salts are stable and convenient to work with, they can be synthesized in only poor yields, which usually lie in the range of 5–10% and have never exceeded 17%, thus far.

(5) The complexation between the π electron density of the chloroarene and an electron-deficient transition-metal center (e.g., the chromium atom in $[Cr(CO)_3]$) dramatically facilitates aromatic nucleophilic substitution.[9] This technique involves the complex preformation, the nucleophilic displacement itself, and, finally, decomplexation which is usually done by the action of an oxidant.

(6) Some very useful transformation of chloroarenes can be performed with stoichiometric amounts of transition metals. Although this method is mostly applied for iodo- and bromoarenes, aryl chlorides also undergo some Ullmann-type transformations[2,10,11] and the Semmelhack reductive coupling to biaryls.[12]

(7) A number of transition-metal complexes catalyze various transformations of aryl chlorides under appropriate conditions.

Each of the above listed methods can be successfully applied for a particularly desired transformation of aryl chlorides. However, the latter technique, employing transition-metal complexes in catalytic quantities, apparently seems to be the most promising and efficient approach to the problem. First, *catalytic* reactions require only small amounts of transition metal complexes, which is definitely advantageous over methods employing *stoichiometric* quantities of transition metals. Second, homogeneous reactions frequently occur with higher selectivities and under milder conditions than heterogeneous transformations. Finally, it is clear now that for many transition-metal-catalyzed transformations, chloroarenes can be used directly, i.e. without any pretreatment, such as complexation with the chromium tricarbonyl framework. In the present review we consider various reactions of chloroarenes, catalyzed by transition-metal complexes, and discuss mechanistic aspects of these transformations.

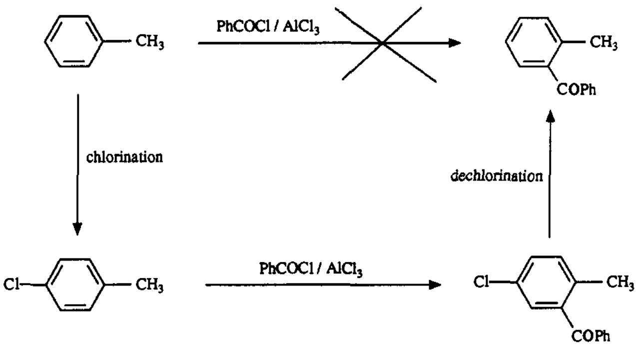
II. Reductive Dechlorination of Chloroarenes

The reductive dechlorination of aryl chlorides (eq 1) is of significant interest for two main reasons. First,

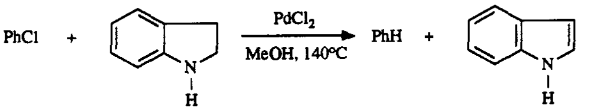
$$ArCl \xrightarrow{[H]} ArH \qquad (1)$$

development of efficient methods for the reduction of the C–Cl bond in chloroarenes is desirable for the neutralization of toxic polychloroaromatics (e.g., polychlorobiphenyls, PCBs) in the environment.[13,14] Second, easy removal of chlorine from aromatic rings can be used in organic synthesis.[15] For instance, it is worth considering chlorine as a protecting group which might offer chemists a unique opportunity to alter the orientation rules of aromatic electrophilic substitution.[16] Scheme 1 illustrates this point, suggesting a route to the selective benzoylation of toluene in the *ortho*-position by protecting the more reactive *para* site against electrophilic attack.[16]

Scheme 1



There are a limited number of methods employing homogeneous transition metal catalysts for the replacement of chlorine for hydrogen in aryl chlorides.[17] The $[Py_3RhCl_3]/NaBH_4$ catalytic system was used for the reduction of chlorobenzene in DMF with H_2 at ambient temperature and atmospheric pressure (ca. 50% conversion with 5 mol % of the catalyst in 13 h).[18] Imai et al.[19] reported the reduction of chlorobenzene with indoline, catalyzed by $PdCl_2$ in methanol (eq 2).



(2)

Among the most interesting features of this process was the striking order of reactivity of halobenzenes: Cl > Br > I, and the fact that the reaction rate did not

Table 1. Reductive Dechlorination of Chloroarenes

chloroarene	reducing agent	catalyst[a] (mol %)	reaction medium[b]	T, °C	reaction time, h	product	yield, %	ref
chlorobenzene	H_2	Rh(5)	A	25	24	benzene	97	22
chlorobenzene	MeOH	Pd(1)	B	100	20	benzene	100	23
chlorobenzene	HCO_2Na	Pd(1)	C	100	20	benzene	90	23
4-chlorotoluene	H_2	Rh(1)	D	60	19	toluene	97	22
4-chlorotoluene	HCO_2Na	Pd(1)	C	150	20	toluene	100	23
3-chlorotoluene	H_2	Rh(1)	D	60	20	toluene	95	22
2-chlorotoluene	H_2	Rh(1)	D	60	18	toluene	7	22
4-chloroanisole	H_2	Rh(1)	D	80	9.5	anisole	99	22
4-chloroanisole	HCO_2Na	Pd(1)	C	150	20	anisole	100	23
4-chloroaniline	H_2	Rh(5)	A	95	19	aniline	91	22
4-chloroaniline	HCO_2Na	Pd(1)	C	100	20	aniline	15	23
1-chloronaphthalene	H_2	Rh(1)	A	85	5	naphthalene	92	22
4-chloro(trifluoromethyl)benzene	H_2	Rh(1)	D	60	18	trifluoromethylbenzene	87	22
3-chlorobenzophenone	H_2	Rh(2)	A	50	3	benzophenone	97	22
4-chloroacetophenone	HCO_2Na	Pd(1)	C	100	20	acetophenone	87	23
4-chlorobenzaldehyde	HCO_2Na	Pd(1)	C	100	20	benzaldehyde	100	23
4-chlorobenzonitrile	HCO_2Na	Pd(1)	C	100	20	benzonitrile	100	23
4-chlorobenzonitrile	MeOH	Pd(1)	B	100	20	benzoic acid	100	23
4-chloronitrobenzene	HCO_2Na	Pd(1)	C	100	20	nitrobenzene	70	23
4-chlorobenzoic acid	H_2	Rh(5)	A	90	25	benzoic acid	99	22
4-chlorophenylacetic acid	H_2	Rh(5)	A	90	21	phenylacetic acid	98	22
carprofen	H_2	Rh(10)	A	90	24	α-methyl-9*H*-carbazole-2-acetic acid	91	22
5-chloro-1-ethyl-2-methylimidazole	H_2	Rh(5)	A	80	8	1-ethyl-2-methylimidazole	97	22
5-chlorobenzodioxole	H_2	Rh(10)	A	90	48	benzodioxole	67	22
tetrachloro-m-xylene	H_2	Rh(20)	A	100	48	2-chloro-*m*-xylene	45	22

[a] Rh = $[(Cy_3P)_2Rh(H)Cl_2]$; Pd = $[Pd(OAc)_2]$/dippp (1:2). [b] A = toluene/40% NaOH/$[Et_3NCH_2Ph]^+Cl^-$; B = MeOH/NaOH; C = MeOH; D = 40% NaOH/$[Et_3NCH_2Ph]^+Cl^-$.

depend on the chlorobenzene concentration. However, while addressing a genuine academic interest, this reaction is not of high practical value due to the high cost of the reducing agent.

For the conversion of chlorobenzene to benzene under mild conditions, magnesium dihydride or sodium hydride was used in THF in the presence of the nickel compounds ($NiCl_2$ or $[(Ph_3P)_4Ni]$)[20] or $[Cp_3La]$,[21] respectively. The lanthanum complex was used in semicatalytic amounts (25 mol %).

Recently, two efficient and convenient procedures for the reductive dechlorination of chloroaromatics were developed (Table 1).[22,23] Several chloroarenes containing various functional groups on the benzene ring were successfully dechlorinated with hydrogen in the presence of the rhodium complexes, $[L_2Rh(H)Cl_2]$,[24] where L = Cy_3P or *i*-Pr_3P. This rhodium-catalyzed hydrogenolysis of the aromatic C–Cl bond occurred readily in the presence of 40% NaOH under exceedingly mild conditions (1 atm of H_2; 25–100 °C) and exhibited broad functional group tolerance.[22] Palladium complexes of dippp catalyzed reduction of aryl chlorides with methanol/alkali or sodium formate at 100–150 °C.[23] Other tertiary phosphine Pd(0) complexes generated in situ from $Pd(OAc)_2$ and the corresponding phosphine L = *i*-Pr_3P, dippb, dippe,[23] and $(PhCH_2)_3P$[26] exhibited catalytic activity for the reduction of chloroarenes with HCOONa[23] or H_2.[26] The best conversions of PhCl to benzene, however, were achieved with the dippp ligand, whereas the triisopropylphosphine complexes of palladium gave the poorest results.[23] A number of functional groups Y remained intact during the $[(dippp)_2Pd]$-catalyzed dechlorination of *p*-YC_6H_4Cl with sodium formate. Both the Rh-[22] and Pd-[23]catalyzed dechlorination processes were found to be highly selective for exclusive arene formation (Table 1).

It is noteworthy that some chloroheteroaromatic compounds with *activated* carbon–chlorine bonds (e.g., 2-chloropyrazines and their *N*-oxide derivatives[27]) can be dechlorinated with HCOONa in the presence of conventional (triphenylphosphine)palladium(0) complexes. Mono- and polychloroarenes were converted into the corresponding cycloalkanes by treatment with H_2, Et_3N, and catalytic amounts of $[Cp^*RhCl_2]_2$.[28] This one-pot procedure involved reduction of the C–Cl bond, followed by hydrogenation of the arenes formed.

III. The Heck-Type Olefination of Chloroarenes

The Heck reaction (eq 3) is a unique method for the single-step arylation of olefins.[29] Unlike aryl iodides and bromides, chloroarenes are usually unreactive under the standard reaction conditions, although it was shown

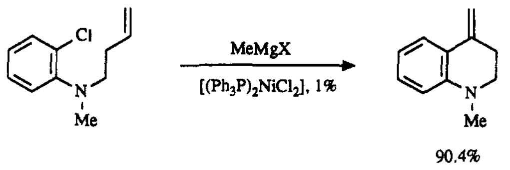
$$ArX + CH_2{=}CHR \xrightarrow[-HX]{[Pd],\ base} ArCH{=}CHR \qquad (3)$$

$$X = \text{halogen}$$

that the stoichiometric reaction between preformed $[(Ph_3P)_2Pd(Ph)Cl]$ and olefins is possible.[30] Both heterogeneous[31] and homogeneous[32,33] catalytic Heck-type arylations with chloroarenes resulted in the desired products in low yield. When the classic catalytic system, $Pd(OAc)_2/Ph_3P$ or *o*-Tol_3P, was applied to the arylation of olefins $CH_2{=}CHZ$ (Z = Ph, CN, $CONEt_2$, CO_2Et) with the aromatic chlorides *p*-YC_6H_4Cl (Y = H, CHO, COMe, CN, NO_2), the corresponding disubstituted olefins were formed in 4–51% yield.[33] Clearly, this catalytic system is limited to electron-withdrawing Y, as the yield was only 4% when Y = H. Under the reaction conditions (DMF, AcONa, 150 °C, 6 h), only

E-isomers were produced, although the arylation of acrylonitrile gave up to 30% of the *Z*-isomer. The limited turnover numbers were likely due to the low reactivity of zerovalent palladium triphenylphosphine complexes toward oxidative addition of the aromatic carbon–chlorine bond. As a result, palladium metal readily precipitated under the reaction conditions, even in the presence of a large excess of PPh_3, and termination of the catalytic process occurred.[33]

A few examples of nickel-catalyzed Heck-type reactions of chloroarenes have been reported.[34–36] Arylation of ethylene[34] and styrene[35,36] with $4\text{-}YC_6H_4Cl$ (Y = H, Me, MeO) in the presence of nickel complexes furnished stilbene[34–36] and its derivatives[36] containing methyl or methoxy groups on the aromatic ring. The originally reported reaction between styrene and chlorobenzene employed the $[(Ph_3P)_2NiCl_2]/Zn$ (excess) system as the catalyst and THF as the solvent.[35] The main product of the reaction was biphenyl, whereas styrene was formed in only 15% yield. Much higher yields of stilbenes (up to 82%) were obtained by conducting the reaction in acetonitrile in the presence of pyridine.[36] Interestingly, it was found[35] that triethylamine, which is commonly used for the Pd-catalyzed Heck-type arylations,[29] inhibited the Ni-catalyzed reaction completely.[37] Mori and co-workers[38,39] reported a number of nickel-catalyzed cyclizations of alkenyl(methyl)(*o*-chlorophenyl)amines involving intramolecular Heck-type arylation of the double bond, furnishing the corresponding N-heterocycles in low[38] to excellent[39] yields (e.g., eq 4).



(4)

An elegant and efficient technique for conducting the Heck reaction of aromatic chlorides was developed by Bozell and Vogt.[40] It was found that ethyl acrylate and acrylonitrile react smoothly with chlorobenzene in the presence of NaI and catalytic amounts of $NiBr_2$, $Pd_2(dba)_3$, and *o*-Tol_3P in DMF, to give *E*-isomers of ethyl cinnamate and cinnamonitrile, respectively. A number of substituted aromatic chlorides were also successfully olefinated in high yields. The reaction occurred via the nickel-catalyzed halogen exchange between ArCl and NaI, followed by the conventional palladium-catalyzed olefination of the iodoarene generated in situ.[40]

Very recently, Milstein and co-workers[41] reported the arylation of styrene and *p*-methoxystyrene with a number of chloroarenes, catalyzed by dippb–palladium complexes. The reaction occurred in DMF at 150 °C, in the presence of NaOAc as a base, giving predominantly *E*-isomers of the substituted stilbenes. No reaction was observed when the DMF solvent was replaced for acetonitrile. Surprisingly, use of Et_3N as the base, again (see above) resulted in substantial retardation of the catalytic process. Palladium complexes of dippp exhibited no catalytic activity under these reaction conditions.[41] However, in the absence of any base and in the presence of zinc powder the (dippp)Pd complexes catalyzed the Heck arylation of styrene with chloroarenes quite efficiently.[42] Interestingly, the formation of *Z*-isomers prevailed in this case. Some examples of Heck-type arylation of olefins with chloroarenes are summarized in Table 2.

IV. Carbonylation of Chloroarenes

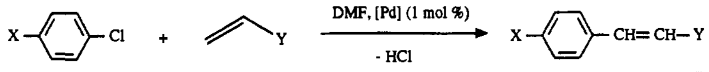
The transition-metal-catalyzed carbonylation of haloarenes is an efficient and simple method for the synthesis of various aromatic carbonyl compounds, such as aldehydes, ketones, carboxylic acids, esters, amides, benzolactams, lactones, etc.[43–46] Both bromo- and especially iodoarenes can be easily involved in this wide range of diverse transformations, which afford valuable carbonyl compounds in very high yields and excellent selectivities. Unfortunately, chloroarenes are far less reactive toward the iron, cobalt, nickel, and palladium complexes which are commonly used for the carbonylation reactions of aryl iodides and bromides.[43–46] Considering the availability of chloroaromatics on an industrial scale, the design and development of new catalytic systems for the carbonylation of aryl chlorides remains one of the most important and challenging problems of modern synthetic organic chemistry.

The first procedures for carbonylation of chloroarenes in the presence of transition-metal compounds were mostly described in the patent literature and required extremely drastic conditions (200–350 °C and 100–300 atm of CO).[47–53] In 1973, Cassar and Foà[54] reported that 1- and 2-chloronaphthalenes could be carbonylated to the corresponding naphthoic acids with $[Ni(CO)_4]$ in the presence of $Ca(OH)_2$ at 110–112 °C and *atmospheric* pressure of CO. The best yields (95–97%) were obtained by running the reaction in DMF, although use of other solvents, such as dimethyl sulfoxide, *N*,*N*-dimethylacetamide, *N*-methylpyrrolidone, and HMPA also gave excellent results. Under the same conditions, chlorobenzene appeared to be 27 times less reactive than 1-chloronaphthalene, 5×10^2 times less reactive than bromobenzene, and 3.25×10^5 times less reactive than iodobenzene.[54] Several palladium-[55,56] and cobalt-catalyzed[57–59] carbonylations of *activated* chloroarenes including 1- and 2-chloronaphthalenes, 1,3,5-trichlorobenzene, 2-chlorothiophene, and 2-chlorofurane were efficiently carried out under mild conditions. The results of mono-[54,57,59] and double[58,59] carbonylation of these substrates, catalyzed by Ni and Co complexes, are summarized in Table 3.

The second important step in the carbonylation of mono- and polychlorinated aromatic hydrocarbons and their derivatives was made by applying photostimulation. Brunet, Sidot, and Caubere[60] succeeded in cobalt carbonyl-catalyzed $S_{RN}1$ carbonylations of *p*-chlorobenzoic and *p*-chlorophenylacetic acids under irradiation (350 nm). The reaction occurred in 5 N NaOH without any organic solvent, leading to the corresponding diacids in 80–98% yield. Following this technique, Kashimura, Kudo, and co-workers[61–64] carbonylated a large number of chloroaromatic compounds including chlorobenzene[64] in the presence of $[Co_2(CO)_8]$ or $Co(OAc)_2{\cdot}4H_2O$, under photochemical conditions (Table 4).

The stoichiometric carbonylation of chlorobenzene (40% conversion) without photostimulation was achieved with the so-called "CoCRACO" system consisting of sodium hydride, sodium neopentoxide, cobalt

Table 2. The Heck-type Olefination of Chloroarenes, Catalyzed by Pd Complexes



X	Y	catalyst[a]	base or reducing agent	T, °C	reaction time, h	yield, % cis	yield, % trans	ref
H	COOEt	A	NaOAc	150	6	0	4	33
H	COOEt	B	Et_3N	140	20–23	0	64	40
H	CN	B	Et_3N	140	20–23	0	50	40
H	Ph	C	NaOAc	150	24	4.4	80	41
H	Ph	D	Zn	140	24	81	7	42
H	Ph	D	Zn	160[b]	24	48	34	42
H	4-MeOC_6H_4	C	NaOAc	150	24	7	70	41
Me	COOEt	B	Et_3N	140	20–23	0	73	40
Me	Ph	C	NaOAc	150	24	5	50	41
OMe	COOEt	B	Et_3N	140	20–23	0	75	40
OMe	Ph	C	NaOAc	150	24	2.2	19	41
OMe	Ph	D	Zn	140	24	37	12	42
OMe[c]	Ph	D	Zn	140	24	46	18	42
CHO	COOEt	A	NaOAc	150	6	0	39	33
CHO	$CONEt_2$	A	NaOAc	150	6	0	45	33
CHO	CN	A	NaOAc	150	6	7	16	33
CHO	Ph	A	NaOAc	150	6	0	37	33
CHO	Ph	C	NaOAc	150	24	5	90	41
COMe	COOEt	A	NaOAc	150	6	0	26	33
COMe	COOEt	B	Et_3N	140	20–23	0	75	40
COMe	Ph	D	Zn	140	24	10	60	42
COOMe	COOEt	A	NaOAc	150	6	0	51	33
COOMe	COOEt	B	Et_3N	140	20–23	0	25	40
COOMe	Ph	D	Zn	160[b]	24	0	65	42
COPh	4-MeOC_6H_4	C	NaOAc	150	24	3	97	41
CN	COOEt	A	NaOAc	150	6	0	32	33
CN	COOEt	B	Et_3N	140	20–23	0	85	40
NO_2	COOEt	A	NaOAc	150	6	0	21	33
NO_2	Ph	C	NaOAc	150	24	8.9	84.6	41

[a] A = $[Pd(OAc)_2]$ + Ph_3P or $p\text{-Tol}_3P$ (1:4); B = $[Pd_2(dba)_3]$ + $o\text{-Tol}_3P$ (1:80), after pretreatment with $NiBr_2$ and NaI (see text); C = $[Pd(OAc)_2]$ + dippb (1:2); D = $[Pd(OAc)_2]$ + dippp (1:2). [b] The reaction was conducted in *N*-methylpyrrolidinone. [c] 3-Chloroanisole.

Table 3. Nickel- and Cobalt-Catalyzed Carbonylation of Activated Chloroarenes at P_{CO} = 1 atm

chloroarene	catalyst (mmol %)	base	solvent	T, °C	reaction time, h	product (yield, %)	ref
1-chloronaphthalene	$[Ni(CO)_4]$ (25)	$Ca(OH)_2$	DMF	110	6	$1\text{-}C_{10}H_7COOH$ (95)	54
1-chloronaphthalene	$[(CO)_4CoCH_2COOEt]$ (2.2)	MeONa	MeOH	25	NR[a]	$1\text{-}C_{10}H_7COOMe$ (67)	57a
1-chloronaphthalene	$[(CO)_4CoCH_2COOMe]$[b] (2–3)	K_2CO_3	MeOH	60	NR	$1\text{-}C_{10}H_7COOMe$ (82)	57a
1-chloronaphthalene	$[(CO)_4CoMe]$[c] (8)	$Ca(OH)_2$	EtOH	20	NR	$1\text{-}C_{10}H_7COCOOH$ (56) $1\text{-}C_{10}H_7COOH$ (20)	58
2-chloronaphthalene	$[Ni(CO)_4]$ (25)	$Ca(OH)_2$	DMF	110	8	$2\text{-}C_{10}H_7COOH$ (97)	54
2-chloronaphthalene	$[(CO)_4CoCH_2COOEt]$ (1.3)	MeONa	MeOH	25	NR	$2\text{-}C_{10}H_7COOMe$ (72)	57a
2-chloronaphthalene	$[(CO)_4CoCH_2COOMe]$[b] (2–3)	K_2CO_3	MeOH	60	NR	$2\text{-}C_{10}H_7COOMe$ (91)	57a
2-chlorothiophene	$[(CO)_4CoCH_2COOEt]$ (1.2)	MeONa	MeOH	25	NR	$2\text{-}(C_4H_3S)COOMe$ (72)	57a
2-chlorothiophene	$[(CO)_4CoCH_2COOMe]$[b] (2–3)	K_2CO_3	MeOH	60	NR	$2\text{-}(C_4H_3S)COOMe$ (98)	57a
2-chlorothiophene	$[(CO)_4CoMe]$[c] (8)	$Ca(OH)_2$	EtOH	20	NR	$2\text{-}(C_4H_3S)COCOOH$ (54) $2\text{-}(C_4H_3S)COOH$ (42)	58
2-chlorofurane	$[(CO)_4CoMe]$[c] (8)	$Ca(OH)_2$	$EtOH/H_2O$	10	NR	$2\text{-}(C_4H_3O)COCOOH$ (41) $2\text{-}(C_4H_3O)COOH$ (34)	58

[a] NR = not reported. [b] Generated in situ from $[Co(CO)_4]^-$ and $ClCH_2COOMe$. [c] Generated in situ from $[Co_2(CO)_8]$ and Me_2SO_4.

acetate, and CO.[65] The chloroarene ligands in $[(ArCl)Cr(CO)_3]$ were carbonylated to various carbonyl compounds in the presence of palladium complexes under mild conditions.[66] A number of carbonyl compounds were obtained by the catalytic reaction of aryl chlorides with carbon monoxide in the presence of Pd salts and bidentate phosphines, such as dppf and dppb at 150–300 °C and 1–200 atm of CO.[67,68] However, no efficient, homogeneously catalytic, nonphotochemical carbonylation of chlorobenzene and other *nonactivated* chloroarenes, under relatively mild conditions, was reported before 1989. Only very recently Huser, Osborn, et al.[69–73] and Ben-David, Portnoy, and Milstein[74–77] reported independently and simultaneously the efficient, palladium-catalyzed carbonylations of chlorobenzene and its derivatives (Table 5). The reactions were generally conducted with Cy_3P[69–73] and dippp,[74–76] although in some cases application of Et_3P,[71] dippb,[74] and dppp[77] also gave satisfactory results. In the presence of H_2 or various nucleophiles, chlorobenzene was catalytically carbonylated to benzaldehyde,[69,71,73,76] benzoic acid,[72,74] alkyl benzoates,[69,70,74] and dialkylbenzamides[73,74] in high yields. The carbonylation of 2-chlorobenzenesulfonamide smoothly gave saccharin in 91.4% yield.[77] When the carbonylations were carried out in the presence of (tricyclohexylphosphine)palladium complexes, higher temperatures and pressures (180 °C, 15–30 bar)[69–73] were employed than in the case of similar reactions catalyzed

Table 4. Carbonylation of Chloroarenes (P_{CO} = 2 atm), Catalyzed by [$Co_2(CO)_8$] (10 mol %), under Photostimulation, *hν* (350 nm)

chloroarene	base	solvent	*T*, °C	reaction time, h	product (yield, %)	ref
C_6H_5Cl[a]	NaOH	H_2O/EtOH	30	20	C_6H_5COOH (49.3)	64
2-$ClC_6H_4CH_3$	NaOMe	MeOH	25–30	92	2-$CH_3C_6H_4COOMe$ (59.3)	63
2-$ClC_6H_4OCH_3$	NaOMe	MeOH	25–30	45	2-$CH_3OC_6H_4COOMe$ (80.4)	63
2-ClC_6H_4Br	NaOMe	MeOH	25–30	40	1,2-$C_6H_4(COOMe)_2$ (97.5)	63
2-ClC_6H_4Br	NaOH	H_2O/EtOH	65	20	1,2-$C_6H_4(COOH)_2$ (24.8) 2-$(COOH)C_6H_4COCOOH$ (9.7) C_6H_5COOH (13.2) 2-ClC_6H_4COOH (40.3–42.8)	62
3-ClC_6H_4Br	NaOH	H_2O/EtOH	65	20	1,3-$C_6H_4(COOH)_2$ (93.7)	61
4-ClC_6H_4Br	NaOH	H_2O/EtOH	65	20	1,4-$C_6H_4(COOH)_2$ (78.9) 4-ClC_6H_4COOH (11.4)	61
2-ClC_6H_4COOH	NaOH	H_2O/EtOH	65	18	1,2-$C_6H_4(COOH)_2$ (34.2) 2-$(COOH)C_6H_4COCOOH$ (29.1) C_6H_5COOH (11.3)	62
2-ClC_6H_4COOMe	NaOMe	MeOH	65	20	1,2-$C_6H_4(COOMe)_2$ (84.4)	63
2-$ClC_6H_4CH_2COOH$	NaOH	H_2O	65	24	2-$(COOH)C_6H_4CH_2COOH$ (87.4) $C_6H_5CH_2COOH$ (3.7)	61
3-ClC_6H_4COOH[a]	NaOH	H_2O	80	2.5	1,3-$C_6H_4(COOH)_2$ (81.6)	64
3-ClC_6H_4COOH	NaOH	H_2O	65	6	1,3-$C_6H_4(COOH)_2$ (94)	61
4-ClC_6H_4COOH	NaOH	H_2O	65	6	1,4-$C_6H_4(COOH)_2$ (93.4)	61
4-ClC_6H_4COOH[b]	NaOH	H_2O	65	8	1,4-$C_6H_4(COOH)_2$ (98)	60
4-$ClC_6H_4CH_2COOH$[b]	NaOH	H_2O	65	15	4-$(COOH)C_6H_4CH_2COOH$ (80)	60
4-$ClC_6H_3(COOH)_2$-1,2	NaOH	H_2O	65	6	1,2,4-$C_6H_3(COOH)_3$ (95)	61
1,2-$C_6H_4Cl_2$	NaOH	H_2O/EtOH	65	24	1,2-$C_6H_4(COOH)_2$ (23) 2-$(COOH)C_6H_4COCOOH$ (12.6) C_6H_5COOH (24.9)	62
1,2-$C_6H_4Cl_2$	NaOMe	MeOH	65	65	1,2-$C_6H_4(COOMe)_2$ (93.8)	63
1,3-$C_6H_4Cl_2$	NaOH	H_2O	65	20	1,3-$C_6H_4(COOH)_2$ (47)	61
1,3-$C_6H_4Cl_2$	NaOH	H_2O/EtOH	65	20	1,3-$C_6H_4(COOH)_2$ (91.6)	61
1,3-$C_6H_4Cl_2$	NaOMe	MeOH	65	36	1,3-$C_6H_4(COOMe)_2$ (87.8)	63
1,4-$C_6H_4Cl_2$	NaOMe	MeOH	65	36	1,4-$C_6H_4(COOMe)_2$ (95.4)	63
1,4-$C_6H_4Cl_2$	NaOH	H_2O/EtOH	65	20	1,4-$C_6H_4(COOH)_2$ (88.4)	61
1,4-$C_6H_4Cl_2$[a]	NaOH	H_2O/EtOH	30	20	1,4-$C_6H_4(COOH)_2$ (66.6) 4-ClC_6H_4COOH (6.5)	64
2,4-$Cl_2C_6H_3COOH$	NaOH	H_2O	65	6	1,2,4-$C_6H_3(COOH)_3$ (13.1) 2-$ClC_6H_3(COOH)_2$-1,4 (40.2) 4-$ClC_6H_3(COOH)_2$-1,2 (13.9) 1,4-$C_6H_4(COOH)_2$ (10.2) 4-ClC_6H_4COOH (23.6)	61
2,4-$Cl_2C_6H_3COOMe$	NaOMe	MeOH	65	45	1,2,4-$C_6H_3(COOMe)_3$ (85.5)	63
3,4-$Cl_2C_6H_3COOH$	NaOH	H_2O	65	6	1,2,4-$C_6H_3(COOH)_3$ (10.8) 2-$ClC_6H_3(COOH)_2$-1,4 (57.3) 1,4-$C_6H_4(COOH)_2$ (14.4) 4-ClC_6H_4COOH (14.6)	61
3,4-$Cl_2C_6H_3COOMe$	NaOMe	MeOH	65	65	1,2,4-$C_6H_3(COOMe)_3$ (87.6)	63
3,5-$Cl_2C_6H_3COOH$	NaOH	H_2O	65	20	1,3,5-$C_6H_3(COOH)_3$ (88.6)	61
4,5-$Cl_2C_6H_2(COOH)_2$-1,2	NaOH	H_2O	65	24	1,2,4,5-$C_6H_2(COOH)_4$ (29.8) 1,2,4-$C_6H_3(COOH)_3$ (52.6)	61
4,5-$Cl_2C_6H_2(COOMe)_2$-1,2	NaOMe	MeOH	65	70	1,2,4,5-$C_6H_2(COOMe)_4$ (85.4)	63
1,2,3-$C_6H_3Cl_3$	NaOMe	MeOH	25–30	92	1,2,3-$C_6H_3(COOMe)_3$ (83.7)	63
1,2,4-$C_6H_3Cl_3$	NaOMe	MeOH	65	70	1,2,4-$C_6H_3(COOMe)_3$ (85.7)	63
1,3,5-$C_6H_3Cl_3$	NaOMe	MeOH	65	40	1,3,5-$C_6H_3(COOMe)_3$ (91.1)	63
1,3,5-$C_6H_3Cl_3$[a]	NaOH	H_2O/EtOH	65	18	1,3,5-$C_6H_3(COOH)_3$ (76.4) 1,3-$C_6H_4(COOH)_2$ (21.3)	64
1,3,5-$C_6H_3Cl_3$	NaOH	H_2O/EtOH	65	20	1,3,5-$C_6H_3(COOH)_3$ (85.5)	61
1,2,4,5-$C_6H_2Cl_4$	NaOMe	MeOH	65	96	1,2,4,5-$C_6H_2(COOMe)_4$ (86.5)	63

[a] $Co(OAc)_2 \cdot 4H_2O$ was used as the catalyst. [b] With 5 mol % of [$Co_2(CO)_8$] and P_{CO} = 1 atm.

by dippp complexes of Pd (120–150 °C, 70–80 psi).[74–76] An exceptionally simple and efficient method was developed for the hydroxycarbonylation of chloroarenes under biphasic conditions (ArCl/20% KOH) in the presence of [$(Cy_3P)_2PdCl_2$] at 100 °C and atmospheric pressure of CO.[78,79]

In concluding this section, it is worth mentioning the report of an efficient, although *heterogeneously* catalyzed (Pd/C in the presence of $K_2Cr_2O_7$), methoxycarbonylation reaction of chlorobenzene and several other chloroaromatics, by Dufaud, Thivolle-Cazat, and Basset.[80]

V. Metal-Catalyzed Nucleophilic Displacement

Since synthetic organic chemistry began, enhancement of the poor reactivity of nonactivated aryl halides toward nucleophiles has been one of the most challenging problems and desirable goals for chemists. Although this problem is still far from being completely solved, significant success has been achieved in promoting aromatic nucleophilic substitution by catalysis with various transition metal complexes. Various copper-assisted nucleophilic substitution reactions of aryl halides (mostly iodides and bromides) will not be

Table 5. Palladium-Catalyzed Carbonylation of Chloroarenes

chloroarene	catalyst[a]	P_{CO}, atm	nucleophile	reaction medium	T, °C	reaction time, h[b]	product	yield, %[b]	ref
C_6H_5Cl	A	15	H_2O	toluene/Et_3N	180	5.5	C_6H_5COOH	88	72
C_6H_5Cl	B	4.8	H_2O	DMF/NaOAc	150	20	C_6H_5COOH	70	74
C_6H_5Cl	C	1	KOH	H_2O	100	72	C_6H_5COOH	89[c]	78, 79
C_6H_5Cl	A	15	MeOH	toluene/Et_3N	180	NR	C_6H_5COOMe	NR[d]	69, 70
C_6H_5Cl	B	4.8	MeOH	DMF/NaOAc	150	20	C_6H_5COOMe	78	74
C_6H_5Cl	B	4.8	MeOH	DMF/Et_3N	150	20	C_6H_5COOMe	71	74
C_6H_5Cl	B	4.8	*n*-BuOH	*n*-BuOH/NaOAc	150	20	C_6H_5COOBu	100	74
C_6H_5Cl	A	15	*n*-$PrNH_2$	toluene/Et_3N	180	11.5	$C_6H_5CONHPr$	NR	73
C_6H_5Cl	B	4.8	Et_2NH	xylene	150	20	$C_6H_5CONEt_2$	72	74
C_6H_5Cl	B	4.8	*n*-Pr_2NH	DMF	150	20	$C_6H_5CONPr_2$	87	74
C_6H_5Cl	B	5.5	HCOONa	DMF	150	20	C_6H_5CHO	90	75, 76
C_6H_5Cl	A	15	H_2 (15 atm)	toluene/Et_3N	180	NR	C_6H_5CHO	NR[e]	69
C_6H_5Cl	D	15	H_2 (15 atm)	toluene/Et_3N	180	NR	C_6H_5CHO	72	72
2-MeC_6H_4Cl	B	5.5	HCOONa	DMF	150	20	2-MeC_6H_4CHO	20	75
2-MeC_6H_4Cl	C	1	KOH	H_2O	100	48	2-MeC_6H_4COOH	65[c]	78, 79
3-MeC_6H_4Cl	C	1	KOH	H_2O	100	48	3-MeC_6H_4COOH	90[c]	78, 79
4-MeC_6H_4Cl	B	4.8	H_2O	DMF/NaOAc	150	20	4-MeC_6H_4COOH	79	74
4-MeC_6H_4Cl	B	5.5	HCOONa	DMF	150	20	4-MeC_6H_4CHO	88	75, 76
4-MeC_6H_4Cl	C	1	KOH	H_2O	100	72	4-MeC_6H_4COOH	116[c]	78, 79
3-$MeOC_6H_4Cl$	B	4.8	*n*-$PrNH_2$	DMF	150	20	3-$MeOC_6H_4CONPr_2$	80	74
4-$MeOC_6H_4Cl$	B	4.8	*n*-BuOH	*n*-BuOH/NaOAc	150	20	4-$MeOC_6H_4COOBu$	75	74
4-$MeOC_6H_4Cl$	B	5.5	HCOONa	DMF	150	20	4-$MeOC_6H_4CHO$	85	75, 76
4-$MeOC_6H_4Cl$	C	1	KOH	H_2O	100	48	4-$MeOC_6H_4COOH$	105[c]	78, 79
4-$MeOCOC_6H_4Cl$	B	4.8	MeOH	DMF/NaOAc	150	20	1,4-$C_6H_4(COOMe)_2$	85	74
3-$PhCOC_6H_4Cl$	C	1	KOH	H_2O	100	48	3-$PhCOC_6H_4COOH$	9[c]	78, 79
4-$CF_3C_6H_4Cl$	C	1	KOH	H_2O	100	72	4-$CF_3C_6H_4COOH$	7[c]	78, 79
2-$CF_3C_6H_4Cl$	E	30	$PhNH_2$	Na_2CO_3	200	3	2-$CF_3C_6H_4CONHPh$	161[c]	68
1-$C_{10}H_7Cl$	C	1	KOH	H_2O	100	72	1-$C_{10}H_7COOH$	103[c]	78, 79
1,4-$C_6H_4Cl_2$	B	4.8	MeOH	DMF/NaOAc	150	20	1,4-$C_6H_4(COOMe)_2$	82	74
2-$ClC_6H_4SO_2NH_2$	F	4.8		dioxane/Et_3N	120	48	saccharin	91.4	77

[a] A = $[Pd(OAc)_2]$ + Cy_3P (1:5), with substrate to Pd ratio = 50; B = $[Pd(dippp)_2]$ or $[Pd(OAc)_2]$ + dippp (1:2), with substrate to Pd ratio = 100; C = $[(Cy_3P)_2PdCl_2]$, with substrate to Pd ratio = 400; D = $[Pd(OAc)_2]$ + Et_3P; E = $[PdCl_2]$ + dppb; F = $[Pd(MeCN)_4](BF_4)_2$ + dppp (1:2), with substrate to Pd ratio = 154. [b] NR = not reported. [c] Ratio: mol of product/mol of Pd. [d] Turnover rate = 1.2 (mol of Pd)$^{-1}$ h^{-1}. [e] Turnover rate = 1.9 (mol of Pd)$^{-1}$ h^{-1}.

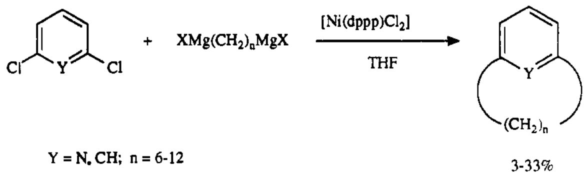
discussed here, since a review on this subject was published several years ago.[10] Among the most recent achievements, it is worth noting the first copper-catalyzed alkoxydechlorination of nonactivated chloroarenes, such as chlorobenzene and 2-chlorothiophene (eq 5).[81] Phase-transfer conditions were successfully

$$ArCl + CF_3CH_2ONa \xrightarrow{CuBr} \underset{70\%}{ArOCH_2CF_3} \qquad (5)$$

Ar = phenyl, 2-thienyl

applied to the copper-catalyzed synthesis of aryl phenyl ethers from chloroarenes and potassium phenoxide.[82] Phenyl(*m*-tolyl) ether was obtained in 100% yield from PhCl and *m*-$CH_3C_6H_4OK$ in the presence of $Cu(OAc)_2$ at 130–149 °C.[83]

Another important area which will not be discussed in detail in the present review is the transition-metal-catalyzed cross-coupling between aryl halides and organometallic carbanion synthons, i.e. replacement of the aromatic halogen for various organic groups. These reactions were investigated by Kharasch and Fields more than 50 years ago.[84] It was later shown[85,66] that tertiary phosphine–nickel complexes are excellent catalysts for the cross-coupling reaction between organic halides and Grignard reagents. Since that time various aspects of diverse cross-coupling processes have been frequently reviewed.[29c,87–97] Regarding the nickel-catalyzed cross-coupling reactions of chloroarenes with organomagnesium compounds, the original papers by Kumada and co-workers[98,99] certainly merit citation (eqs 6 and 7).



(6)

$$ArCl + RMgX \xrightarrow[Et_2O]{[Ni]} \underset{6\text{–}100\%}{Ar\text{–}R} \qquad (7)$$

Ar = C_6H_5, 2-$CH_3C_6H_4$, 3-$CH_3C_6H_4$; 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-$CF_3C_6H_4$;

R = CH_3, C_2H_5, *n*-C_3H_7, *i*-C_3H_7, *n*-C_4H_9, c-C_6H_{11}, c-C_3H_5, $(CH_3)_3SiCH_2$, 2,4,6-$(CH_3)_3C_6H_2$, $CH_2{=}C(CH_3)$

Among recent accomplishments in this area it is worth mentioning the nickel-catalyzed cross-coupling between polychlorobiphenyls and Grignard reagents,[100] the cross-coupling of various RMgX with haloarenes (including PhCl) catalyzed with $NiCl_2$ in the absence of tertiary phosphines,[101] and the synthesis of butylbenzene from PhCl and BuZnCl in the presence of $[(Ph_3P)_2NiCl_2]$.[102]

Most cross-coupling reactions of aryl chlorides require nickel complexes as the catalyst, because the metal

Table 6. Nickel-Catalyzed Nucleophilic Substitution in Chloroarenes

chloroarene	nucleophile	Ni catalyst[a] (mol %)	solvent	T, °C	reaction time, h	product (yield, %)	ref
C_6H_5Cl	KCN	A (8)[b]	C_6H_5Cl	45	17	C_6H_5CN (90)	107
C_6H_5Cl	KCN	B (3.3)	HMPA	60	6	C_6H_5CN (94)	108
1-$C_{10}H_7Cl$	NaCN	C (0.8)[c]	H_2O	55	12.5	1-$C_{10}H_7CN$ (96)	107
2-$C_{10}H_7Cl$	NaCN	C (1.6)[c]	C_6H_6/H_2O	55	16	2-$C_{10}H_7CN$ (90)	107
4-MeC_6H_4Cl	KCN	A (4)[b]	4-MeC_6H_4Cl	55	25	4-MeC_6H_4CN (86)	107
3-MeC_6H_4Cl	KCN	B (3.3)	HMPA	60	6	3-MeC_6H_4CN (95)	108
2-MeC_6H_4Cl	KCN	B (3.3)	HMPA	60	16	2-MeC_6H_4CN (86)	108
4-$MeOC_6H_4Cl$	NaCN	C (1.6)[c]	H_2O	55	14	4-$MeOC_6H_4CN$ (96)	107
4-$MeOC_6H_4Cl$	KCN	B (3.3)	MeCN	50	6	4-$MeOC_6H_4CN$ (92)	108
4-$MeOC_6H_4Cl$	KCN	B (3.3)	HMPA	60	6	4-$MeOC_6H_4CN$ (92)	108
3-$MeOC_6H_4Cl$	KCN	B (3.3)	HMPA	60	6	3-$MeOC_6H_4CN$ (97)	108
2-$MeOC_6H_4Cl$	KCN	B (3.3)	HMPA	60	16	2-$MeOC_6H_4CN$ (96)	108
3-FC_6H_4Cl	KCN	B (3.3)	HMPA	60	6	3-FC_6H_4CN (99)	108
1,3-$C_6H_4Cl_2$	NaCN	A (1.6)[c]	C_6H_6/H_2O	55	4.5	1,3-$C_6H_4(CN)_2$ (50) 3-ClC_6H_4CN (16)	107
1,2-$C_6H_4Cl_2$	KCN	B (3.3)	HMPA	60	16	1,2-$C_6H_4(CN)_2$ (7) 2-ClC_6H_4CN (3)	108
4-$CF_3C_6H_4Cl$	KCN	B (3.3)	HMPA	60	6	4-$CF_3C_6H_4CN$ (81)	108
3-$CF_3C_6H_4Cl$	KCN	B (3.3)	MeCN	50	6	3-$CF_3C_6H_4CN$ (46)	108
4-CNC_6H_4Cl	KCN	B (3.3)	MeCN	50	6	1,4-$C_6H_4(CN)_2$ (95)	108
3-CNC_6H_4Cl	KCN	B (3.3)	MeCN	50	6	1,3-$C_6H_4(CN)_2$ (69)	108
2-CNC_6H_4Cl	KCN	B (3.3)	HMPA	60	6	1,2-$C_6H_4(CN)_2$ (21)	108
C_6H_5Cl	PhSNa	C (5.4)	toluene	55	20	$(C_6H_5)_2S$ (70)	113
C_6H_5Cl	PhSK	D	*N*-methylpyrrolidinone	80	10	$(C_6H_5)_2S$ (13)	114
C_6H_5Cl	KI	E	HMPA	150	12	C_6H_5I (13)	115
C_6H_5Cl	Me_2NH	F (1)	EtOH	210	6	$C_6H_5NMe_2$ (68)	117
4-$Me_2NC_6H_4Cl$	Ph_3P	G (10)	EtOH	78	24	$[4\text{-}Me_2NC_6H_4PPh_3]^+Cl^-$ (58)	118

[a] A = $[(Et_3P)_3Ni]$; B = $[(Ph_3P)_2NiBr_2]$ + Zn + Ph_3P; C = $[(Ph_3P)_2Ni(1\text{-}C_{10}H_7)Cl]$ + Ph_3P; D = $[NiBr_2]$ + Zn + dppf; E = $[NiBr_2]$ + Zn + *n*-Bu_3P; F = $[NiCl_2]$; G = $[(Ph_3P)_3Ni]$. [b] In the presence of dicyclohexano-18-crown-6. [c] In the presence of Aliquat 336.

center in Ni(0) compounds readily undergo oxidative addition of the carbon–chlorine bond (see below). Zerovalent complexes of palladium usually exhibit negligible catalytic activity in cross-coupling reactions of chloroarenes even in the best ligand cases. For instance, coupling of chlorobenzene with phenylboronic acid is not catalyzed by $[(Ph_3P)_4Pd]$. When conducted in the presence of $[(dppb)PdCl_2]$, this reaction produced biphenyl, although in only 28% yield.[103] It is noteworthy that heteroaryl chlorides with activated C–Cl bonds were much more reactive under similar conditions, giving good to excellent yields of the coupling products.[103]

The transition-metal-promoted replacement of an aromatic halogen for a cyano group is commonly realized in the presence of stoichiometric amounts of Cu(I) compounds.[104] In 1973 Cassar[105] reported that chloroarenes could be converted to the corresponding nitriles in the presence of NaCN and *catalytic* quantities of $[(Ph_3P)_4Ni]$. This reaction was later intensively studied under both homogeneous[106] and phase-transfer[56,107] conditions. Sakakibara and co-workers[108] found some of Cassar's procedures[106] employing alcohol as the solvent often irreproducible, and obtained good to excellent yields of nitriles from the corresponding chloroarenes by running the nickel-catalyzed cyanations in MeCN or HMPA. Cobalt complexes were found to be much less efficient for the cyanation of chloroarenes. Thus, the cobalt-catalyzed reaction of 1-chloronaphthalene with the CN^- led to 1-naphthyl cyanide in only 18% yield.[109] Although efficient in the cyanation of aryl iodides, bromides, and triflates,[110] palladium complexes do not catalyze displacement of Cl^- in ArCl by CN^-, unless the carbon–chlorine bond is activated (e.g., in chloropyrazines).[111] The palladium- or nickel-catalyzed synthesis of benzonitrile from chlorobenzene and inorganic or organic cyanates in the presence of CO was patented by Harris.[112]

Other nucleophiles which can be utilized in the metal-promoted displacement of chlorine in chloroarenes include phenylthiolate[113,114] and iodide[115,116] anions, primary and secondary amines,[117,118] and tertiary phosphines.[119,120] All reactions are catalyzed by either preformed or generated in situ Ni(0)–phosphine complexes. Examples are given in Table 6.

VI. Miscellaneous Reactions

In 1971 Semmelhack, Helquist, and Jones[12] reported the stoichiometric synthesis of biaryls from aryl halides and $[(COD)_2Ni]$. Unlike the Ullmann reaction,[2] the Ni(0)-promoted reductive homocoupling of haloarenes proceeds under exceedingly mild conditions. The reaction was rendered catalytic through successful reduction of nickel(II) halides back to the Ni(0) species during each catalytic cycle. Various biaryls and biheteroaryls were obtained from the corresponding chloroarenes and chloroheteroarenes, respectively, in the presence of the reducing agent, zinc, and catalytic amounts of nickel phosphine or bipyridyl complexes (eq 8).[121-124] Originally, the yields were modest,[121] but

$$2\text{ArCl} + \text{Zn} \xrightarrow{[(\text{Ph}_3\text{P})_2\text{NiCl}_2]} \text{Ar–Ar} + \text{ZnCl}_2 \tag{8}$$

were dramatically improved by thorough optimization of the reaction conditions and catalyst systems.[123,124] The catalytic reaction can also be conducted electrochemically.[125-128]

The palladium-catalyzed coupling of terminal acetylenes with chloroarenes occurs only if the C–Cl bond is activated toward oxidative addition by an electron-withdrawing group on the ring (e.g., eq 9).[129]

$$p\text{-}NCC_6H_4Cl + HC{\equiv}CPh \xrightarrow[\text{DMF, 80 °C, 8 h}]{[(Ph_3P)_4Pd],\ MeONa} p\text{-}NCC_6H_4C{\equiv}CPh \quad (9)$$

64%

A very interesting catalytic reaction of chlorobenzene was very recently reported by Petrov et al.[130] Red phosphorus reacted with PhCl in PCl_3 containing catalytic amounts of $PdCl_2$, CuCl, S, or S_2Cl_2, to give phenyldichlorophosphine in ca. 50–60% yield (eq 10).

$$P_{(red)} + PhCl \xrightarrow[390\ °C]{PCl_3/cat} PhPCl_2 \quad (10)$$

Regarding the synthesis of organophosphorus compounds directly from phosphorus and inexpensive chloroarenes, reaction 10 is of significant importance, despite requiring quite drastic conditions (390 °C).

VII. Mechanistic Studies and Considerations

The first key step in all above described catalytic reactions is the metal complex activation and cleavage of the aromatic carbon–chlorine bond. Kinetic factors are in disfavor of the carbon–chlorine bond cleavage in chlorobenzene (see above). Nevertheless, a number of low-valent transition metal complexes can rupture the C–Cl bond in nonactivated chloroarenes. For instance, some compounds of Co (I),[131] Mo (0),[132] Rh (I),[133-135] Ir (I),[133,134,136,137] Pt (0),[138-141] Y (0),[142] Sm (0),[142] U (III)[143,144] are capable of cleaving the C–Cl bond in chlorobenzene or *p*-chlorotoluene. However, for a number of reasons these reactions could hardly be used for the creation of a catalytic cycle involving aryl chlorides or other organic substrates. The oxidative addition of ArCl to Rh(I), Ir(I), and Pt(0) compounds results in the formation of stable M(III) (M = Rh, Ir) octahedral or Pt(II) square-planar σ-aryl complexes which are too unreactive for an efficient catalytic utilization. In the rest of the cases, metal complex catalyst recycling does not seem to be possible. Due to the specific subject of this review, we will consider here only those activations of the C–Cl bond which subsequently can result in *catalytic* transformations of chloroarenes. Most attention will be focused on the reactions of aryl chlorides with the nickel, palladium, and cobalt complexes. Mechanistic aspects of the carbon–chlorine bond cleavage in the course of the rhodium-catalyzed hydrogenolysis of chloroarenes will also be considered.

A. Nickel and Palladium Complexes

The reactivity of zerovalent d^{10} complexes $[L_nM]$, where L = tertiary phosphine and n = 2, 3, 4, toward chlorobenzene (eq 11) significantly decreases in the

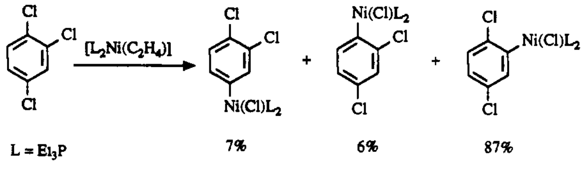
$$[L_nM] + ArHal \rightarrow [L_2M(Ar)Hal] + (n-2)L \quad (11)$$

L = tertiary phosphine, R_3P; n = 2, 3, 4;
M = Ni, Pd, Pt; Hal = I, Br, Cl

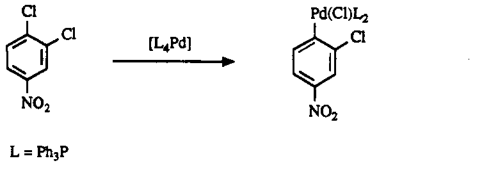
order Ni > Pd > Pt, other things being equal.[138,145,146] Although only qualitative data are available, the difference in reactivity of similar nickel, palladium, and platinum complexes is quite well-pronounced. For example, the oxidative addition of PhCl to $[(Et_3P)_3Pt]$ requires refluxing of the reactants in toluene for 15 min, whereas the reaction between $[(Et_3P)_3Ni]$ and chlorobenzene proceeds instantly at ambient temperature.[138] Similarly, the reaction of $[(Cy_3P)_2Ni]$ with PhCl at 20 °C was complete in 3 h,[147] while 4 days at room temperature were necessary for the reaction of chlorobenzene with bis(tricyclohexylphosphine)platinum.[139] The reactivity of tertiary phosphine palladium complexes toward oxidative addition of aryl halides is appreciably less than that of isoelectronic and isostructural nickel compounds, and significantly higher than the reactivity of similar platinum analogues.[145,146]

Both R and n play the crucial role for the oxidative addition of aryl halides to the complexes $[(R_3P)_nM]$, where M = Ni, Pd, and Pt. Under comparable conditions, chloroarenes react with $[(Ph_3P)_3Ni]$ at a considerably lower rate than with $[(Et_3P)_3Ni]$,[148-150] and the same is observed for analogous platinum complexes.[138] Oxidative addition of chlorobenzene to $[L_n\text{-}Pd]$ complexes is much more facile when L is an electron-rich alkylphosphine like Cy_3P[69,79] or *i*-Pr_2*n*-BuP[151] than when L = Ph_3P.[152,153] The palladium complexes of basic, *chelating* trialkylphosphines are substantially more reactive toward chlorobenzene than their nonchelating analogues.[151,154,155] The influence of the chelate effect on the structure of electron-rich Pd(0) complexes and their ability to oxidatively add the carbon–chlorine bond of various chloroarenes was studied in detail by Portnoy and Milstein.[151] It was shown that the reactivity toward PhCl decreases in the order $[(dippp)_2Pd] > [(i\text{-}Pr_2n\text{-}BuP)_3Pd] \gg [(dippe)_2Pd] \gg [(dppp)_2Pd]$. The latter two complexes are not prone to opening up their stable chelates, and the resulting lack of coordinative unsaturation makes the reaction with PhCl sluggish. In contrast with this, the chelating ability of dippb and dippp is substantially lower, which results in much higher reactivity of their Pd(0) complexes toward chlorobenzene.[151]

In his early work, Fahey[156] showed that the selectivities of the oxidative addition of chloroarenes to Ni(0) and Pd(0) complexes (eqs 12 and 13) were similar to those observed earlier for the classic organic S_NAr reactions with the same aromatic substrates. Thus, it was reasonable to have concluded that these oxidative addition reactions proceed by an S_NAr pathway.[156,157]



(12)



(13)

A few years later Foà and Cassar[149] thoroughly studied oxidative addition of various aryl chlorides to $[(Ph_3P)_3\text{-}$

Ni] and made a number of important observations. By measuring relative rate constants, it was firmly established that strong electron-withdrawing groups X in 4-XC_6H_4Cl facilitate the reaction. For the substituents X with Hammett's $\sigma > 0.23$, a high ρ value of 8.8 was found, revealing that the oxidative addition process is very sensitive to substituent effects. However, almost no difference in reactivity was observed for all substrates whose X substituents' σ constants were lower than 0.23. For instance, *p*-dichlorobenzene ($\sigma_{p\text{-Cl}} = 0.23$) and 4-chlorophenyl phenyl ether ($\sigma_{p\text{-OPh}} = -0.32$) were equally reactive toward the Ni(0) complex. In addition, the 4-XC_6H_4Br were approximately 100 times more reactive than the corresponding 4-XC_6H_4Cl when X was a strong electron acceptor; however, the difference in reactivity dropped down to just 2–3 for electron-donating substituents X. All these observations could be accounted for by mechanistic changes. In fact, it was proposed[149] that an unsymmetrical three-center transition state mechanism is operative, which can approach an S_NAr-type mechanism for substrates containing electron-withdrawing substituents. Equations 14–16 were suggested in order to accommodate

$$[L_3Ni] \rightleftarrows [L_2Ni] + L \tag{14}$$

$$[L_3Ni] + ArCl \rightarrow [L_2Ni(Ar)Cl] + L \tag{15}$$

$$[L_2Ni] + ArCl \rightarrow [L_2Ni(Ar)Cl] \tag{16}$$

$$L = PPh_3$$

the observed first-order kinetics with respect to the substrate and the fact of significant retardation of the reaction by extra triphenylphosphine. The bis(phosphine) species is much more reactive than the starting tricoordinate complex.

Tsou and Kochi[150] studied the reaction between $[(Et_3P)_4Ni]$ and various haloarenes by kinetic, electrochemical, and spectral (ESR) means indicating a single electron transfer mechanism. It was found that both Ni(II) and paramagnetic Ni(I) complexes result from the interaction of the Ni(0) complex and aryl halides (eq 17).

$$[L_4Ni] + ArHal \rightarrow [L_2Ni(Ar)Hal] + [L_3NiHal] \tag{17}$$

$$L = Et_3P$$

The Ni(I)/Ni(II) ratio was strongly dependent on the solvent, substituents attached to the aromatic ring, and the nature of the halogen (Hal). However, for aryl *chlorides* the ratio was always zero under any conditions, with the exception of the trimethyl(*p*-chlorophenyl)ammonium cation which reacted with the $[L_4Ni]$ to give 32% of the halonickel(I) complex. Nevertheless, evidence was found for a common reaction intermediate regardless of the nature of Hal in the substrate. First, there was a strong correlation between substituent effects on the reaction rates of aryl iodides, bromides, and chlorides. Second, it became clear from the study of solvent effects that the Ni(I) and Ni(II) products did not result directly from the rate-limiting activation process. Third, the influence of added halonickel(I) complex on the yield of the paramagnetic species and the reaction rate indicated that the formation of the Ni(I) and Ni(II) complexes must have occurred subsequent to the rate-limiting step. The mechanism (eqs 18–20) involves slow, single electron transfer as the rate-limiting step, to give the tight ion pair, $[L_3Ni^+ ArX^{-\bullet}]$.

$$[L_4Ni] \rightleftarrows [L_3Ni] + L \tag{18}$$

$$[L_3Ni] + ArHal \rightarrow [L_3Ni^+ HalAr^{\bullet-}] \tag{19}$$

$$[L_3Ni^+HalAr^{\bullet-}] \left\{ \begin{array}{l} \xrightarrow{\mathbf{A}} [L_2Ni(Ar)Hal] + L \\ \xrightarrow{\mathbf{B}} [L_3Ni]^+ + Hal^- + Ar^\bullet \end{array} \right. \tag{20}$$

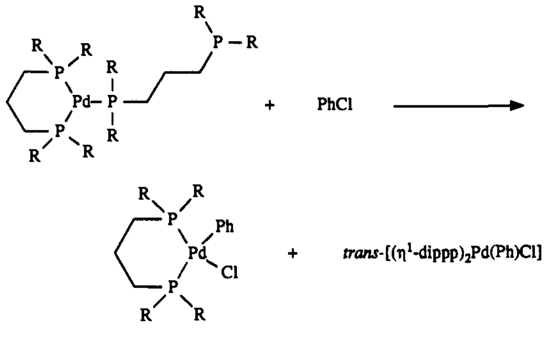
$$L = Et_3P$$

Depending on which path (**A** or **B**, eq 20) dominates, various Ni(I) to Ni(II) ratios are obtained. When Hal = Cl, path **B** is disfavored due to the high energy of homolysis of the C–Cl bond in the corresponding radical anion. The ρ value (+5.4) obtained by Tsou and Kochi[150] with triethylphosphine–Ni(0) complexes is close to the $\rho = +8.8$ calculated for the oxidative addition of ArCl to $[(Ph_3P)_3Ni]$[20] (see above). Therefore, it was suggested[150] that the triphenylphosphine nickel complex reactions with chloroarenes might be of relevance to the electron transfer mechanism. It is not clear at this time, whether or not a concerted mechanism[145,149,156–158] and the single electron transfer path[150,159] can be independently and separately operative in the reactions of tertiary phosphine–Ni(0) complexes with aromatic chlorides.[160]

Mechanistic studies of oxidative addition reactions between triphenylphosphine–Pd(0) complexes and aryl halides (mostly iodides), have been carried out by several research groups.[145,161–164] However, the low reactivity of nonactivated chloroarenes, including chlorobenzene,[152] toward $[(Ph_3P)_nPd]$ (n = 2, 3, 4) makes the oxidative addition of the C–Cl bond inconvenient for mechanistic investigations. Some (tricyclohexylphosphine)palladium(0) complexes, such as $[(Cy_3P)_2Pd(dba)]$[69] and $[(Cy_3P)Pd]$ (which is presumably generated from $[(Cy_3P)_2PdCl_2]$ in the presence of aqueous alkali),[79] readily undergo oxidative addition of PhCl under mild conditions (60–100 °C). For instance, the $[(Cy_3P)_2Pd(dba)]$ reacts smoothly with PhCl at 60 °C to furnish the σ-phenyl complex, $[(Cy_3P)_2Pd(Ph)Cl]$ in 76% isolated yield after 2 h.[69] Other chloroarenes, *p*-XC_6H_4Cl (X = NO_2, COOEt, OCH_3), react similarly, with the reactivity decreasing in the order $NO_2 > COOEt \gg H > OCH_3$. Interestingly, Pd(0) analogues containing electron-rich but bulkier phosphine ligands (*t*-Bu_3P and *t*-Bu_2PhP), or those of similar steric volume but lower basicity ($CyPh_2P$, *m*-Tol_3P), did not give the corresponding expected adducts with PhCl under the same conditions. Mechanisms of the oxidative addition of chloroarenes to the (tricyclohexylphosphine)palladium(0) complexes have not been studied.

The first publication describing a purposeful mechanistic study of chloroarene oxidative addition to Pd(0) complexes, appeared only very recently. Portnoy and Milstein[154] demonstrated that the reaction between $[(dippp)_2Pd]$ and PhCl readily occurs in dioxane at 90

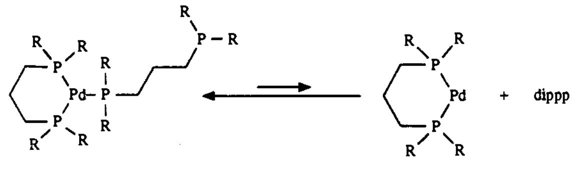
°C, to give two adducts, viz. *cis*-[(dippp)Pd(Ph)Cl] and *trans*-[(η^1-dippp)$_2$Pd(Ph)Cl] (eq 21).



(21)

R = i-Pr$_3$P

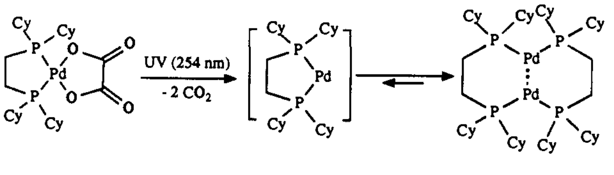
The *cis* and *trans* σ-phenyl complexes, which originally form independently, are in equilibrium with each other. The equilibrium is shifted to the *cis* isomer which is also favored kinetically. The reaction rate is solvent-dependent and increases in the order hexane < dioxane ≈ THF < DMF. Although the reaction is first order in chlorobenzene, it is only approximately first order in the palladium(0) complex, perhaps due to the equilibrium between [(dippp)$_2$Pd] and the dinuclear complex, [(dippp)$_2$Pd$_2$(μ-dippp)]. The rate-determining step in the formation of the *cis*-σ-phenylpalladium complex is the oxidative addition of the C–Cl bond to the 14-electron Pd(0) intermediate, [(dippp)Pd], which was shown to exist in the equilibrium with the original tricoordinate complex (eq 22).



(22)

R = i-Pr$_3$P

Equation 22 is in accord with the observation that the oxidative addition reaction slows down significantly in the presence of extra dippp. This fact, along with the results of the inversion transfer NMR experiment, provide strong support for existence of a 14-electron Pd(0) species in solution. What remains unknown is the structure of [(dippp)Pd]. In light of the recent communication by Pan, Mague, and Fink,[155] this question could appear to be more complicated than it seems upon initial consideration. It was reported that the loss of CO_2 from [(dcpe)Pd(C_2O_4)] under UV-irradiation in acetonitrile results in smooth formation of [(dcpe)$_2$Pd$_2$] in 85% isolated yield.[155] The reaction is likely to proceed via the photochemically generated intermediate [(dcpe)Pd], followed by its instantaneous dimerization (eq 23). A single-crystal X-ray diffraction study of the Pd(0) product revealed an unusual dinuclear structure with the Pd–Pd bond length equal to 2.7611(5) Å.



(23)

Chlorobenzene (as well as some other reagents) oxidatively adds to the dimer, to furnish the σ-aryl mononuclear compound [(dcpe)Pd(Ph)Cl], which is formed as though a [(dcpe)Pd] *monomer* were the reacting complex. It was, therefore, reasonable to propose an equilibrium between the monomer, [(dcpe)-Pd], and its well-characterized dimer.[155] As both the cone angle and basicity of Cy$_3$P are very close to those of *i*-Pr$_3$P,[165] one could anticipate a certain similarity in the same parameters between dcpe and dippp (although their chelating properties should be different). Therefore, in addition to the mechanistic scheme suggested by Portnoy and Milstein,[154] it is worth considering participation of an equilibrium between the [(dippp)-Pd] and [(dippp)$_2$Pd$_2$], with the latter possessing a structure similar to that of the [(dcpe)$_2$Pd$_2$].

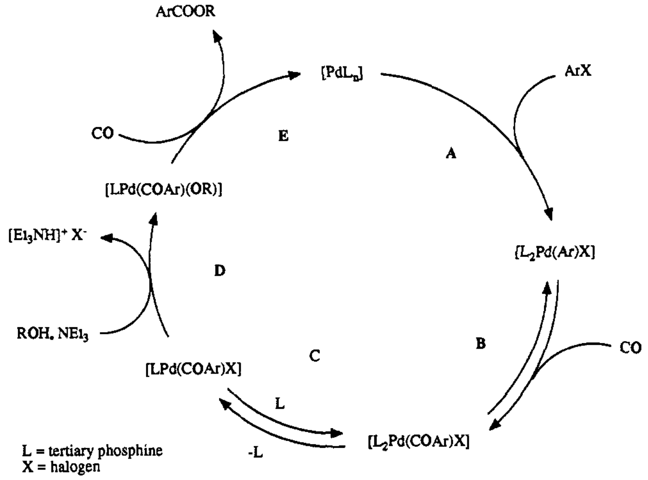
Rate constants for the oxidative addition of a series of ArCl to [(dippp)$_2$Pd] were measured and found to correlate well with the Hammett σ^- constants ($\rho = +5.2$), but not with σ. On the basis of this data and the activation parameters obtained, it was concluded that an S$_N$Ar-type charged transition state with partial coordination of the chlorine atom to the metal center is operative in the reaction.

It is interesting to compare the reactivities of dippp–Ni(0) and –Pd(0) complexes toward chlorobenzene. The ^{31}P NMR spectra of the reaction mixtures resulting from the Ni(0)–dippp complexes and aryl chlorides pointed in a number of cases to the formation of Ni(I) paramagnetic impurities.[166] In contrast, nothing similar was observed when the analogous Pd(0) complex reacted with the same substrates.[154] This difference in the chemical behavior of the Ni(0) and Pd(0) complexes was taken as one of the arguments in favor of an S$_N$Ar-type mechanism operating in the oxidative addition to the Pd center, rather than the one-electron transfer scheme suggested by Tsou and Kochi.[150] On the other hand, it is known that all Pd(I) complexes are diamagnetic possessing di- or polynuclear structures with the metal–metal bond.[167] It is worth noting here that one such complex, [(dippp)$_2$Pd$_2$(μ-H)(μ-CO)], was obtained from the reaction between [(dippp)Pd(Ph)-Cl] and MeOH in the presence of Et$_3$N, and fully characterized, including X-ray analysis.[168]

From the material discussed above, it is now quite clear as to how a palladium or nickel complex should be designed for the facile activation and cleavage of the carbon–chlorine bond in nonactivated chloroarenes. However, to successfully cleave the C–Cl bond does not mean to solve completely the problem of the creation of the catalytic cycle. In other words, the C–Cl bond activation is one of the key steps on the way to catalytic transformations of aryl chlorides, but there are other, subsequent key steps to be realized in order to make the catalytic reaction work. Unfortunately, it is quite common when a transition-metal complex is capable of cleaving the carbon–chlorine bond but, at the same time, fails to serve as a catalyst. With respect to this problem, it is appropriate to quote here the following dictum by Portnoy and Milstein: "A problem frequently encountered in the design of catalytic cycles is that what is good for one step is detrimental for another, e.g. the conflicting requirements of oxidative addition and insertion or the reductive elimination reaction."[154] For instance, many tertiary phosphine–Ni(0) complexes easily cleave the C–Cl bond of chloroarenes at ambient and even lower temperatures (see above). Nonetheless, these complexes cannot be used for catalytic carbonylations of chloroarenes (or other substrates) simply because in the presence of CO they are converted to the stable carbonyl phosphine species, e.g., $[(R_3P)_2Ni(CO)_2]$. The latter is too stable to be sufficiently reactive toward the substrate and therefore appear to be catalytically inactive. On the contrary, some other Ni(0) complexes, such as $[Ni(CO)_4]$[54] and $[Ni(CO)_3CN]^-$,[169] readily catalyze the carbonylation of various organic halides, but not nonactivated chloroarenes, owing to their insufficient reactivity toward the C–Cl bond.

It is reasonable to assume that the palladium catalyzed carbonylation of chloroarenes proceeds via a mechanism similar to that proposed for analogous reactions of bromo- and iodoarenes (Scheme 2).[146,170,171]

Scheme 2

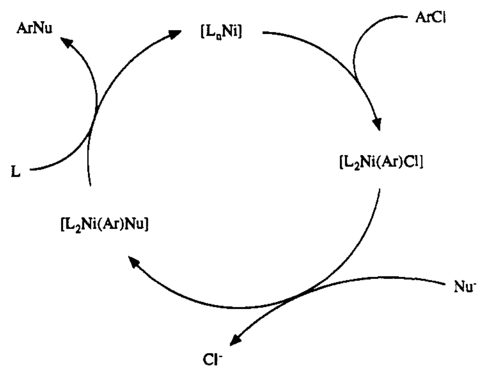


As seen from Scheme 2, the nature of the halogen X might influence all but one (**E**) single step of the catalytic cycle. These are: (i) oxidative addition of the Ar–X bond to the Pd(0) species (path **A**); (ii) the carbonylation of the σ-arylpalladium complex to the corresponding aroyl complex (paths **B** and **C**); (iii) the base-assisted alcoholysis of the aroyl species (path **D**). It is certainly worth considering how the catalytic intermediates originating from the oxidative addition of the Ar–Cl bond differ in reactivities from the corresponding complexes formed by the reactions with the Ar–Br and Ar–I bonds. While the ease of the oxidative addition of ArX (path **A**) is strongly dependent on X, this does not seem to be the case with the following steps **B**, **C**, and **D**. As it was shown by Garrou and Heck,[146] the rate of carbonylation of σ-aryl–Pd(II) complexes, $[L_2Pd(Ar)X]$, only slightly depends on the nature of the halogen X (less than a factor of 2), whereas electronic properties of both Ar and L are much more influential. Ozawa et al.[170] demonstrated that the reaction of the aroyl intermediate, $[(Ph_3P)_2Pd(COPh)X]$, with EtOH in the presence of triethylamine proceeds almost equally fast, regardless of X. Under the same conditions, the observed rate constant ratio was found to be 3.75:3.46:3.25 for X = I, Br, and Cl, respectively. Oxidative addition was found to be the rate-determining step in the Pd-catalyzed alkoxycarbonylation reaction of bromobenzene, but not of iodobenzene whose reaction with the Pd(0) complex is much more facile.[172] From all these data one would have anticipated that, in the carbonylation of chlorobenzene under similar conditions, oxidative addition of the C–Cl bond should be the rate-determining step. In other words, it is the oxidative addition of the C–Cl bond to a Pd(0) complex which seems to be the most problematic step in the carbonylation of chloroarenes with monodentate phosphine palladium complexes. Surprisingly, it was found that Ph–Cl bond activation with (tricyclohexylphosphine)palladium complexes is comparatively facile, not being the rate-limiting step of the catalytic alkoxy- or hydrocarbonylation of chlorobenzene.[69] Perhaps step **B** is less facile and straightforward in the case of (tricyclohexylphosphine)-palladium complexes. Indeed, the carbonylation of $[(Cy_3P)_2Pd(Cl)Ph]$ requires 30 bar of CO at room temperature and is reversible at 60 °C under argon,[69] whereas its triphenylphosphine analogue, $[(Ph_3P)_2Pd(Cl)Ph]$, is rapidly and irreversibly carbonylated under atmospheric pressure at ambient temperature.[146] It was also found that the facility of carbonylation of the platinum complexes $[(Ph_3P)_2Pt(C(CH_3){=}CH_2)X]$ decreased dramatically in the order $X = I > Br > Cl$.[173] Therefore, it is conceivable that, under certain circumstances, the nature of the halogen in the organic substrate can play an important role not only at the stage of oxidative addition but also at the following stages of the catalytic cycle. There is no precise data on the influence of both X and L (Scheme 2) on the ligand exchange resulting in the aroylalkoxy complex which undergoes reductive elimination of the ester. In fact, the catalytic cycle for the Pd-catalyzed carbonylation of haloarenes might well be more complicated than the reaction sequence depicted in Scheme 2, since it was recently shown[66c,79,168] that *dinuclear* palladium complexes likely participate in the process.

When palladium complexes of bidentate phosphines are used for the catalytic functionalization of chloroarenes, a proper choice of the phosphine ligand for each particular process is critical. Although dippp is the best ligand for various Pd-catalyzed carbonylations[74–77] and reduction[23] of aryl chlorides, it does not work at all when applied to the Heck arylation of olefins with ArCl in the presence of base.[41] At the same time, the latter process is readily catalyzed with the Pd complex of dippb[41] which exhibits much weaker catalytic activity in other transformations of chloroarenes. Such a remarkable difference in the catalytic activities of the palladium dippp and dippb complexes is likely due to the requirement of one extra coordination site for the Heck reaction to occur. The dippb Pd complexes readily undergo the chelate opening, thus creating the coordinative unsaturation required, whereas the dippp Pd chelate is not prone to do so, making the complex catalytically inactive in the aryl chloride olefination reaction.[41]

A few mechanistic points deserve to be made concerning the nickel-catalyzed nucleophilic displacement reactions and C–C reductive coupling of chloroarenes. It is likely that the Ni(0) promoted S_N-reactions of aryl chlorides proceed according to the catalytic cycle shown in Scheme 3.

Scheme 3



L = tertiary phosphine

Nu$^-$ = CN$^-$, RS$^-$, etc.

The reaction usually requires excess phosphine which substantially facilitates the reductive elimination step. An interesting example found by Cassar[105] (eq 24)

$$[(Ph_3P)_2Ni(o\text{-}ClC_6H_4)CN] \left\{ \begin{array}{l} \xrightarrow{PPh_3} \text{no reaction} \\ \xrightarrow{dppe} \underset{70\%}{o\text{-}ClC_6H_4CN} \end{array} \right. \quad (24)$$

illustrates how the nature of the extra phosphine affects the reductive elimination. No reaction was observed when the σ-arylnickel cyano complex [(Ph$_3$P)$_2$Ni(o-ClC$_6$H$_4$)CN] was treated with triphenylphosphine. However, in the presence of dppe, smooth and clean reductive elimination occurred to give o-chlorobenzonitrile in 70% yield.

Tsou and Kochi[116] assigned Ni(I) complexes as the active catalyst in the halogen exchange between haloarenes and halide anions. It was found that direct halide exchange between aryl halides and arylnickel(II) halides involves a radical-chain process with an induction period. The radical reaction is inhibited by quinones and nitroarenes.

Numerous reports were published on C–C coupling reactions of organonickel complexes (see ref 174 and references cited therein). It is most likely that the reaction involves a disproportionation of [L$_2$Ni(Ar)Cl] to [L$_2$NiCl$_2$] and [L$_2$Ni(Ar)$_2$], followed by reductive elimination of the biaryl from the latter complex.

B. Cobalt and Rhodium Complexes

An S$_{RN}$1-type mechanism was proposed for the photochemical cobalt carbonyl catalyzed carbonylation of aryl halides under phase-transfer conditions.[60,175] The proposed mechanism involves the σ-arylcobalt carbonyl species generation, followed by the aryl ligand migration to one of the carbonyl ligands and subsequent nucleophilic cleavage of the aroyl complex thus formed. Obviously, the most intriguing step in these carbonylation reactions is the cobalt-induced cleavage of the carbon–halogen bond. Brunet, Sidot and Caubere[60] suggested the following scheme for the initiation step (eqs 25–29):

$$ArX + [Co(CO)_4]^-M^+ \rightleftarrows [ArX,Co(CO)_4^-,M^+] \rightleftarrows [ArX,Co(CO)_4^-,M^+]^* \quad (25)$$

$$[ArX,Co(CO)_4^-,M^+]^* \rightarrow [ArX^{\bullet-},Co(CO)_4,M^+] \rightarrow [Ar^\bullet,{}^\bullet Co(CO)_4,M^+,X^-] \quad (26)$$

$$\begin{aligned} [Ar^\bullet,{}^\bullet Co(CO)_4,M^+,X^-] \rightarrow [ArCo(CO)_4] &+ MX \\ &\hookrightarrow \text{carbonylation} \end{aligned} \quad (27)$$

or

$$[Ar^\bullet,{}^\bullet Co(CO)_4,M^+,X^-] \xrightarrow{[^\bullet Co(CO)_4]} [Co_2(CO)_8] + Ar^\bullet + MX \quad (28)$$

$$\begin{aligned} Ar^\bullet + [Co(CO)_4]^-M^+ \rightarrow [ArCo(CO)_4]^{\bullet-},M^+ &\xrightarrow{ArX} [ArCo(CO)_4] + ArX^{\bullet-} + M^+ \\ &\hookrightarrow \text{carbonylation} \end{aligned} \quad (29)$$

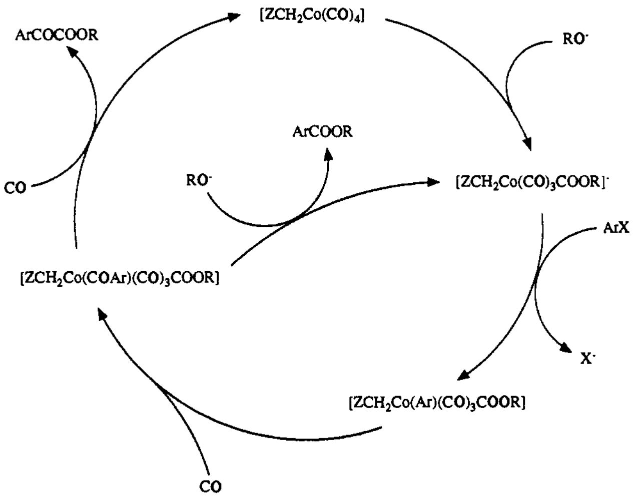
Under the reaction conditions, some substrates (e.g., p-bromophenol) gave very poor yields of the corresponding carbonylation products, and at the same time, did not undergo dehalogenation.[60] Thus, it was concluded that the aryl radical was strongly held inside the cobalt carbonyl reactive complex and did not escape from the cage. The photolysis of aryl bromides as the initiation step for the carbonylation was ruled out by Brunet et al.[60] However, Kashimura and co-workers clearly demonstrated that the carbon–halogen bond in some aryl iodides and bromides can be easily cleaved under the reaction conditions in the absence of the cobalt complex, to give the corresponding arene.[63] In the presence of the catalyst, [Co$_2$(CO)$_8$], the reduction process was substantially suppressed. This fact provides additional support for the hypothesis that the aryl radical does not leave a solvent cage during the photochemical catalytic carbonylation. It is noteworthy that aryl bromides and especially iodides are much more inclined to C–Hal bond homolysis than chloroarenes.

Some relatively reactive chloroarenes, such as chloronaphthalenes, chlorothiophene, and chlorofurane, can be carbonylated in the presence of alkylcobalt carbonyl catalysts without irradiation.[57–59] It is believed that the reaction follows the catalytic cycle presented in Scheme 4.

The key catalytic species, [ZCH$_2$Co(CO)$_3$COOR]$^-$, possesses enhanced reactivity toward the aromatic carbon–halogen bond, cleaving it presumably via a single electron-transfer mechanism.[57,59] The reactive anionic complex is formed by nucleophilic attack of the alkoxide anion on a carbonyl ligand of [ZCH$_2$Co(CO)$_4$], which can be either used as preformed added catalyst (Z = COOR′, F, CN, etc.), or generated in situ from [Co(CO)$_4$]$^-$ and CH$_3$I or (CH$_3$)$_2$SO$_4$ (Z = H). Scheme 4 readily accounts for the formation of mono- and dicarbonylated products.

Utilization of rhodium complexes in catalytic transformations of chloroarenes is limited, in fact, by few examples of the carbon–chlorine bond hydrogenolysis.[18,22,28] It was originally found that complexes [L$_2$Rh(H)Cl$_2$] (L = Cy$_3$P or i-Pr$_3$P), in the presence of hydrogen and alkali, transform to a species which can easily activate the C–H bond in benzene.[176] This

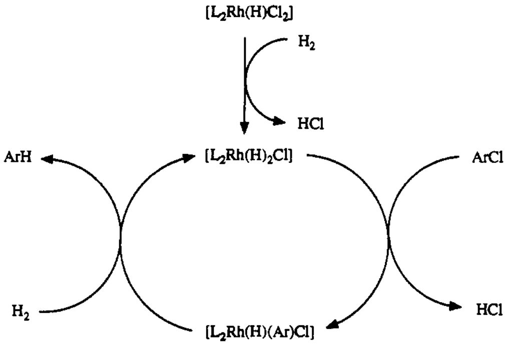
Scheme 4



Z = H, $COOCH_3$, $COOC_2H_5$, F, CN, $C_6H_5Cr(CO)_3$

observation led logically to the application of the system for the catalytic hydrogenolysis of the C–Cl bond in chloroarenes.[22] The catalytic cycle is based on continuous formation of chlorohydridorhodium complexes and their decomposition through loss of HCl.[22] Although the proposed formal mechanism (Scheme 5) looks quite plausible, it is rather oversimplified as the process most likely involves participation of η^2-H_2 rhodium species which were established by ^1H NMR in systems consisting of the starting Rh monohydrides, H_2, and alkali.[176] It is noteworthy that isostructural and isoelectronic iridium complexes, $[L_2Ir(H)Cl_2]$ (L = i-Pr_3P, Cy_3P), react with H_2 in the presence and absence of alkali to give a number of classical and nonclassical polyhydrides, which were thoroughly characterized in solution and in the solid state.[177,178] Therefore, it is conceivable that some similar but far less stable rhodium species might be formed under the same conditions, with some of them being responsible for the C–Cl bond hydrogenolysis.

Scheme 5



VIII. Conclusions and Future Perspectives

As seen from the above described material, considerable progress has been achieved on the functionalization of chloroarenes via catalysis with transition metal complexes. Probably the most exciting and promising discovery of recent years in this area is the successful application of palladium catalysis for the carbonylation of aryl chlorides. With this discovery, it has been demonstrated that proper design and choice of tertiary phosphine ligands make it possible to extend an exceedingly rich catalytic chemistry of palladium to various transformations of chloroarenes. One could expect this area of research to develop in several principal directions. First, it is important to synthesize new ligands and palladium complexes which could be used for already known catalytic transformations of chloroaromatics. For instance, it was very recently shown[179] that palladium complexes of some chelating bis(phosphine) ligands containing 2-methoxyphenyl substituents are efficient catalysts for chloroarene carbonylations under mild conditions. Second, it is worth exploring the possibility of applying known palladium complexes for new catalytic conversions of aryl chlorides. Third, mechanistic studies should accompany the practical research in order to better understand how the catalytic system should be designed for successful application to the chemistry of aromatic chloro compounds.

IX. Abbreviations

Ac	acetyl
Ar	aryl
Bu	butyl
Cp	cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
Cy	cyclohexyl
dba	dibenzylideneacetone
dcpe	1,2-bis(dicyclohexylphosphino)ethane
dippb	1,4-bis(diisopropylphosphino)butane
dippe	1,2-bis(diisopropylphosphino)ethane
dippp	1,3-bis(diiospropylphosphino)propane
DMF	*N,N*-dimethylformamide
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
Et	ethyl
HMPA	hexamethylphosphoramide
Me	methyl
Ph	phenyl
Pr	propyl
Py	pyridine
THF	tetrahydrofuran
Tol	tolyl

X. References

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(24) In fact, added catalyst was a nonstoichiometric mixture of cocrystallized $[L_2Rh(H)Cl_2]$ and $[L_2RhCl_2]$, obtained from the reaction between rhodium trichloride hydrate and L in 2-propanol.[22] The Rh(II) nonhydrido complex was shown to react in a facile manner with H_2 in solution to give the monohydride $[L_2Rh(H)Cl_2]$.[25]

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(37) In a number of cases, the nickel-catalyzed reaction between ArX and $RCH{=}CH_2$ led to significant amounts (up to 45%) of the saturated product, RCH_2CH_2Ar.[35] Having established that the *extra* hydrogen atoms did not originate from the solvent (THF), the authors[35] failed to account for the source of hydrogen in their reaction system. In our opinion, it is conceivable that the originally formed arylolefins were catalytically reduced with zinc/hydrogen halide. The Zn was used in a large excess for the reaction, while the hydrogen halide must have been produced in equimolar quantities during the arylation process, which was conducted in the *absence* of base.[35] Perhaps, the key reduction step involved acidolysis of the σ-complex, $[(ArCH_2CHR)Ni(PPh_3)_2X]$, with HX to give the saturated product ($ArCH_2CH_2R$), with regeneration of the added catalyst, $[(Ph_3P)_2NiX_2]$.

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