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Metal-Mediated Reductive Hydrodehalogenation of Organic Halides

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I. Introduction

A. Organic Halides: Historical Overview

Organic halides are very important and versatile compounds with many applications as starting materials, solvents, reagents, and intermediates in synthetic organic chemistry.[1] One of the first organic halides synthesized was trichloroacetaldehyde, by Liebig in 1832. Its hydrated form is commonly called chloral,[2a] recently considered a safe and effective substance,[2b] with hypnotic properties. It is key reagent in the synthesis of the powerful insecticide DDT [1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane].[2] Since then, and parallel to the development of organic synthetic methods, a plethora of organic halides, with different properties and applications, have been synthesized.[3] For instance, during the First World War many of the toxic gases used were chlorine-based compounds, including asphyxiating gases such as chloropicrine (CCl_3NO_2),[4a,b] diphosgene ($ClCOOCCl_3$),[4c,d] and phosgene ($COCl_2$),[4d,e] lacrimatory agents such as chloroacetone[4f] and chloroacetophenone,[4g] or vesicant gases such as the mustard gas $[(ClCH_2CH_2)_2S]$[4h,i] and lewisite ($ClCH{=}CHAsCl_2$).[4j,k]

Acyclic short-chain organic halides have been widely used as solvents, the principal representatives being the chlorinated solvents methylene chloride[5a] (applied in pharmaceuticals, chemical processing, aerosols, and surface treatment including paint stripping and urethane foam blowing), tetrachloroethylene[5b] (dry and metal cleaning), and trichloroethylene[5c] (metal cleaning and specialty adhesives). Fortunately, these solvents have a low impact on the environment, with a relatively short atmospheric lifetime, 6−8 days (trichloroethylene) and 5−6 months

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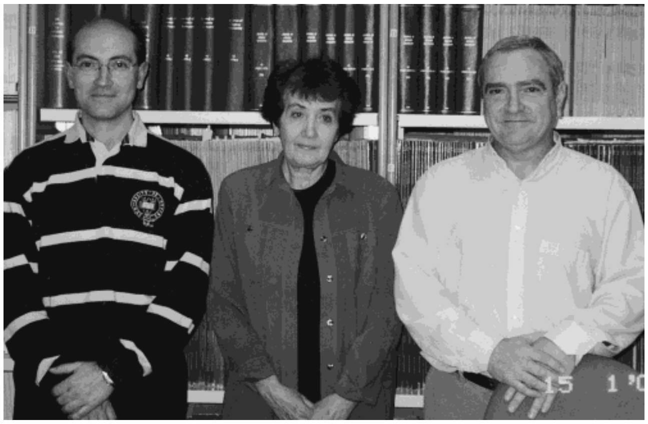


Miguel Yus (right) was born in Zaragoza in 1947. He received his B.Sc. (1969), M.Sc. (1971), and Ph.D. (1973) degrees from the University of Zaragoza. After spending two years as a postdoctoral student at the Max Planck Institut für Kohlenforschung in Mülheim a.d. Ruhr, he returned to the University of Oviedo, where he became Associate Professor in 1977, being promoted to Full Professor in 1987 at the same university. In 1988 he moved to a chair in organic chemistry at the University of Alicante, where he is currently the head of the Organic Chemistry Department. Prof. Yus has been visiting professor at different institutions such as ETH-Zürich and the Universities of Oxford, Harvard, Uppsala, Marseille, Tucson, Okayama, and Paris VI. He is a member or fellow of the chemical societies of Argentina, England, Germany, Japan, Spain, Switzerland, and the United States. He is coauthor of more than 250 papers, mainly in the field of the development of new methodologies involving organometallic intermediates in synthetic organic chemistry. Among others, he has recently received the Spanish-French Prize (1999), the Japan Society for the Promotion of Science Prize (2000), and the Stiefvater Memorial Lectureship Award (2001).

Irina P. Beletskaya (middle) received her Diploma degree in 1955, her Ph.D. degree in 1958, and her Doctor of Chemistry degree in 1963 from Moscow State University. The subject of her thesis for the latter was electrophilic substitution at saturated carbon. She became a Full Professor in 1970 and in 1974 a Corresponding Member of the Academy of Sciences (USSR), a full member (Academician) of which she became in 1992. She is currently Head of the Laboratory of Organoelement Compounds, Department of Chemistry, Moscow State University. Dr. Beletskaya is Chief Editor of the *Russian Journal of Organic Chemistry*. She was President of the Organic Chemistry Division of IUPAC from 1989 to 1991. She was a recipient of the Lomonosov Prize (1979), the Mendeleev Prize (1982), and the Nesmeyanov Prize (1991). She is the author of over 500 articles and 4 monographs. Her current scientific interests are focused on (i) transition-metal catalysis in organic synthesis, (ii) organic derivatives of lanthanides, and (iii) carbanions and nucleophilic aromatic substitution.

Francisco Alonso (left) was born in Villena (Alicante) in 1963. He received his B.Sc. (1986), M.Sc. (1988), and Ph.D. (1991) degrees in chemistry from the University of Alicante. After a postdoctoral stay (1992–1994) as a Fleming fellow at the University of Oxford, U.K., with Prof. S. G. Davies, he moved back to the University of Alicante and joined the research group of Prof. Yus. He became Associate Professor in 1998, and his research interest has focused on the development of new synthetic methodologies involving active metals and the application of organometallic intermediates to the synthesis of naturally occurring molecular structures. He was awarded with the Ph.D. Extraordinary Prize in 1992.

(tetrachloroethylene and methylene chloride), not being regulated by the Montreal Protocol. Furthermore, methylene chloride is completely biodegradable under both aerobic and anaerobic conditions, whereas trichloroethylene and tetrachloroethylene display much slower biodegradation, especially under anaerobic conditions, and for this reason, there is an urgent need to understand their transport and to develop effective control methods.[5d−f] There is some evidence that high doses of trichloroethylene and tetrachloroethylene can cause cancer in experimental animals, and the International Agency for Research on Cancer (IARC) has determined that both are probably carcinogenic to humans.[5g]

In the 1940s the industry of chlorinated insecticides reached maximum production and development, lindane,[6a] aldrin,[6b] and dieldrin[6c] representing the most important members of this family. But special mention must be made of DDT.[6d] Its use in the control of insect-borne disease has saved many millions of lives over the first half of the past century, chiefly through the decimation of the *Anopheles* mosquito, the main carrier of the parasite that causes malaria. Although its toxicity toward mammals is low (the fatal human dose is about 500 mg/kg of body weight), DDT is very resistant to biodegradation. Its accumulation in the food chain makes it a hazard to birds and fish, and consequently it has been banned by the U.S. Environmental Protection Agency (EPA) since 1972. Nevertheless, due to its effectiveness and low cost it remains the chemical of choice for combating mosquitoes in some malaria-infested areas of the world. Both lindane[6e,f] and DDT[6g−i] have been anticipated to be carcinogenic compounds.

Organic halides can also exist in polymeric form; such is the case for poly(vinyl chloride) (PVC),[7a−c] poly(tetrafluoroethylene) (PTFE),[7d] or neoprene.[7e] These materials have found multiple applications and are present in many items of diary use. It is worthy to note the remarkable applications of PVC as well as the controversy this material has aroused in recent years, above all in the toy industry. There is a vast array of PVC products including luggage, shoes, raincoats, umbrellas, fabric and paper coatings, computers and keyboards, magnetic recording tape, recreational equipment, inflatable boats and water floats, baby stroller furnishings, food packaging, garden hoses, lawn furniture, floor and wall coatings, blood storage materials, and more. PVC is useful because it resists water and fire (chlorine atoms inhibit combustion). However, its production is carried out by free radical polymerization of vinyl chloride, and exposure to this monomer has been linked to the incidence of a rare form of liver cancer called angiocarcinoma. The Occupational Safety and Health Administration (OSHA) has set limits of human exposure to vinyl chloride of less than an average of 1 ppm per 8 h working day per worker.[7f−h]

Not all the man-made organic halides have shown a deleterious effect either on the environment or in living organisms. In fact, there is a large list of halogenated compounds whose therapeutic applications have saved many lives, contributing to improvement of the welfare of society, and enlarging the half-life expectation. Among them, we can highlight the synthetically modified nucleic acid base fluracil (antineoplasic),[8a,b] antifungal fluconazole,[8c,d] antidepressant fluoxetine (better known by the brand name Prozac),[8e,f] antihistaminic chlorpheniramine,[8g] antimicrobial chlorhexidine,[8h,i] and peripheral vasodilator brovincamine.[8j,k]

Moreover, Nature itself has been able to synthesize an endless collection of halogenated organic compounds (more than 1500 chlorine-containing chemicals).[9a−d] Thus, they are produced by seaweeds, algae, assorted plants, some vegetables and fruits, fungi and mushrooms, lichen, microorganisms, marine creatures, frogs, insects, and even some mammals. They show diverse biological activities and some of them medicinal properties. This is the case for chloramphenicol (chloromicetin),[9e] isolated from the cultures of the soil bacterium *Estreptomyces venezuelae*, or vancomycin,[9f] produced by *Estreptomyces orientalis*, both with antibacterial activity and very effective in treating typhus, meningitis, urinal infections, brucellosis, or certain viruses. Basidiomycetes, as decomposers of forest litter, represent an ecologically important group of organisms in the environment and are known to produce and degrade a wide variety of organohalogen compounds.[9g−i] Halogenated secondary metabolites are especially abundant in the red algae of the genera *Laurencia*[9j] and *Plocamium*,[9k] as well as in some lichens[9l] and marine sponges.[9m,n] Many of these compounds have represented an important challenge as targets for synthetic organic chemists.[9o,p] One of the few natural molecules in the human body containing a halogen is the thyroid hormone thyroxin, with four carbon−iodine bonds.[9q,r] A superb and highly recommended review by Winterton on the chemistry and biochemistry of chlorine in the natural world has been recently published.[9s]

B. Present Environmental Concern

In the past decade the preservation of the environment has been a major concern for governments,[10a] academic and research institutions,[10b−e] industry,[10f] ecological associations,[10g] and, in general, the whole society.[10g,h] Thus, a series of new policies to regulate and control the production, emission, waste treatment, and disposal of organic halogenated materials have recently emerged. Nevertheless, nowadays there is still a special emphasis focused on the potential effects of three of the most recalcitrant toward degradation types of halogenated compounds: chlorofluorocarbons (CFCs), chlorinated dibenzo-*p*-dioxins (dioxins), and polyhalogenated biphenyls (PCBs and PBBs). All of them deserve a previous comment, since many reports included in this review will tackle their transformation in less damaging derivatives.

CFCs[11a,b] are nontoxic, nonflammable chemicals used in the manufacture of aerosol sprays and blowing agents for foams and packing materials and as solvents and refrigerants. However, in 1974, Rowland and Molina[11c] showed that UV photolytic decomposition of the CFCs could be a major source of inorganic chlorine in the stratosphere, affecting the ozone layer in catalytic reactions where 100000 molecules of ozone can be destroyed per chlorine atom. A loss of stratospheric ozone results in more harmful UV-B radiation reaching the Earth's surface, which could cause biological damage in plants, animals, and human beings. A large depletion of stratospheric ozone was described in 1985 by Farman and his colleagues[11d] and was called "the Antartic ozone hole" by others.[10h]

In 1987, 27 nations signed a global environmental treaty, the Montreal Protocol to Reduce Substances that Deplete the Ozone Layer,[11e] that had a provision to reduce 1986 production levels of these compounds by 50% before the year 2000. An amendment approved in London in 1990 was more forceful and called for the elimination of production by the year 2000. The chlorinated solvents methylchloroform (CH_3CCl_3)[11f] and carbon tetrachloride (CCl_4) were added to the London Amendment.

The environmental concern for CFCs follows from their long atmospheric lifetime [55 years for CFC-11 (CCl_3F) and 140 years for CFC-12 (CCl_2F_2)],[11g] which limits our ability to reduce their abundance in the atmosphere and the associated future ozone loss. This resulted in the Copenhagen Amendment that further limited production and was approved later in 1992. The manufacture of these chemicals ended for the most part on Jan 1, 1996. A total of 148 signatory countries have now signed the Montreal Protocol. Atmospheric measurements of CFC-11 and CFC-12 reported in 1993 showed that their growth rates were decreasing as a result of both voluntary and mandated reductions in emissions.[11g,h]

The demand for CFCs was accommodated by the use of substitutes such as hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs).[11i,j] The advantage of using HCFCs is that the hydrogen reacts with tropospheric hydroxyl (OH), resulting in a shorter atmospheric lifetime. However, HCFCs still contain chlorine, which makes it possible for them to destroy ozone. The Copenhagen Amendment calls for their production to be eliminated by the year 2030. The HFCs are considered one of the best substitutes for reducing stratospheric ozone loss because of their short lifetime and lack of chlorine.

Dioxins[12] are probably the environmental contaminants with the worst reputation.[10i] In fact, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) is considered as "the most toxic man-made chemical", 500 times more toxic than strichnine and 100000 times more toxic than sodium cyanide. The following effects[10e,12d] have been associated with exposure to this compound: (a) lethal effects at very low concentrations (one millionth of a gram kills a guinea pig); (b) immune system damage at similar levels in all animals examined; (c) damage to other organs such as the liver, kidney, and digestive tract; (d) reproductive effects (miscarriage, sterility); (e) birth defects, including neurological effects; (f) cancer, 2,3,7,8-TCDD being the most potent cancer promoter known; (g) chloracne,[12e] producing persistent skin eruptions in humans and some animals. 2,3,7,8-Tetrachlorodibenzofuran (2,3,7,8-TCDF) shows almost the same toxicity.[12a,b]

Chlorinated dioxins and furans are generated, and therefore can be emitted to the atmosphere during combustion of municipal and chemical wastes,[12f,g] but also running motor-vehicle engines and wood burning are sources of dioxins.[12h,i] They are also present as byproducts in chlorinated aromatic compounds. For instance, 2,3,7,8-TCDD was present as an impurity in the so-called Agent Orange, a 1:1 mixture of the butyl esters of 2,4,5-trichlorophenoxyacetic acid and its 2,4-dichloro analogue, used in large amounts as a defoliant during the Vietnam war. Exposure of

Vietnam veterans to 2,3,7,8-TCDD (in Agent Orange) has been connected with low sperm count, increased incidence of miscarriage in their wives, and a wide variety of organ malformation in children. A certain number of deformed babies have been born in Vietnam since Agent Orange was used there.[12d] On the other hand, some epidemiologic studies[12j−l] concluded that no human illness, other than chloracne, which occurred only in highly exposed people, has been associated with dioxin.

Due to the controversy around dioxins, in 1994 the EPA embarked upon a research program to further evaluate the exposure of Americans to this class of compounds. This program is called The Dioxin Exposure Initiative. Parallel to the development of this program, the EPA released the public review draft of the Dioxin Reassessment Documents, which has been revised and updated.[12d,m] Similar initiatives have been undertaken by the European Comission.[12n−p]

Polychlorinated biphenyls (PCBs)[13] consist of a mixture of different congeners and isomers (209 PCBs are possible altogether) that have been employed for several decades in transformer dielectric fluids, as coolants, and in carbonless copy paper, due to their thermal stability, flame retardancy, and other chemical inertness. However, their reluctant behavior to degradation and tendency to accumulate in animal tissue (they have also been found in breast milk) have curtailed their applications, and they are no longer produced. Degradation by incineration has some limitations, since it has been associated with increased levels of dioxins, furans, and PCBs in the environment. With regard to health effects, higher exposure to PCBs during pregnancy has been linked to miscarriages and lower scores on the psychomotor scale. It is believed that they may cause toxemia by affecting the immune system. Moreover, there is evidence of synergistic effects between 2,3,7,8-TCDD and one PCB congener in causing birth defects. However, no association between high levels of PCBs and breast cancer has been found.[13c]

Polybrominated biphenyls (PBBs)[13a] are also serious environmental contaminants[14a−c] with documented cyto- and genotoxicity,[14d,e] as well as long-term health effects.[14f] Recent studies estimated their half-life in the body to be about 11 years and showed their possible association with breast cancer.[14g] As an example, in a person infested with 46 ppb of PBB it is estimated to take over 60 years for this level to fall below the current detection level of 1 ppb.[14h]

It can be concluded that new efforts are in progress in the scientific community in industry, academia, and government to have an informed understanding and risk assessment of the thousands of halogenated compounds (and chlorinated compounds in particular) in use today.

C. Reactivity of the Carbon−Halogen Bond

Taking into account the general resistance to degradation of organic halogenated materials, substantial budgets have been invested in the development of efficient methods and techniques to properly treat this type of compound.[15a] Inactivation by oxidation methods and incineration[15b−g] is related to the production of some noxious chemicals. Therefore, reductive methods can be considered as an alternative to be taken into account prior to their safe but controversial incineration. Among them, electrochemical,[16] photochemical,[17] ultrasonic,[18] microbial,[19] and radiolytic and thermal[20] reductive methods have been reported.

In general, chemical methods have been by far the most studied ones.[21] The chemical reduction of organic halides involving the replacement of halogen by hydrogen is the so-called hydrogenolysis of the carbon−halogen bond or hydrodehalogenation reaction. The paramount importance of this reaction has attracted much attention from all chemists in general, and from organic chemists in particular, among other reasons due to its application in practical organic synthesis. The large variety of reducing systems developed hitherto practically guarantees the existence of a specific reagent for a specific substrate, to successfully carry out this type of transformation. Therefore, the method of choice will depend mainly on the characteristics of the substrate, that is to say, the nature of the carbon−halogen involved, hybridization at the halogen-bearing carbon, substituent effects, and the presence of other halogens or functional groups.

It is well known that the ease of reductive hydrodehalogenation of organic halides follows the general order $I > Br > Cl \gg F$. This order is related to the dissociation energy of carbon−halogen bonds (C−I, 53 kcal mol^{-1}; C−Br, 67 kcal mol^{-1}; C−Cl, 81 kcal mol^{-1}; C−F, 109 kcal mol^{-1}).[22] This difference makes possible the selective hydrodehalogenation reaction in di- or polyhalides containing different halogen atoms. Due to the strength of the C−F bond, fluorides are rather resistant to reduction, though many efforts have been made to overcome its chemical inertness by appropriate activation.[23]

Concerning the structure of the substrate, the cleavage of the carbon−halogen bond is favored in the order aliphatic[24a] < aromatic[24b] < vinylic[24b] < allylic[24c] < benzylic.[24c] The reactivity of primary, secondary, and tertiary halides is very dependent on the reagent employed, the steric environment affecting the rate of the reduction. In general, primary halides are the most easily reduced when the process involves an S_N2 mechanism or in catalytic hydrogenation, whereas the trend is just the opposite when the reaction proceeds through an S_N1 mechanism, or with the participation of free radicals as intermediates, the reduction following the sequence tertiary > secondary > primary. The latter behavior is also observed with complex hydrides, where the reagent is a strong electrophile. The carbon−halogen bond is especially reactive in α-halocarbonyl compounds.[24d]

The most important chemical methods[21] to accomplish the hydrodehalogenation of organic halides are catalytic hydrogenation,[25a] reduction with metals or low-valent metal compounds,[25b] reduction with metal hydrides or complex metal hydrides,[25c,d] and reduction with some strong nucleophilic neutral or anionic species.[25e,f] Although several reviews[21−25] have been published regarding the use of the above-mentioned methods and reagents, most of the references therein are prior to 1990. For this reason, the aim of this review is to cover a wide range of different contributions to the metal-mediated hydrodehalogenation reaction published since 1990, other methods being excluded due to the huge dimensions the review would reach. It must be noted that to provide a complete survey on the title topic, we have considered of interest to include methodologies involving not only metals in the zerovalent state, but also organometallic species and certain metal-containing inorganic compounds. The organization and presentation order of all the information collected on this topic was the main difficulty to face for the following reasons: (a) many different types of substrates (including monohalogenated and polyhalogenated substrates) are tackled regarding the nature of the carbon−halogen bond (C−F, C−Cl, C−Br, C−I), hybridization and substitution pattern at the halogen-bearing carbon atom, presence of other functional groups, etc.; (b) a vast range of reducing agents are used for the title process with different modes of action; (c) a variety of mechanisms are involved depending on the type of substrate, reducing agent, and reaction conditions, which in some cases remain unclear or are ambiguous; (d) the aims pursued by the different research groups are also diverse (i.e., hydrodehalogenation from a synthetic point of view or as a destruction methodology of hazardous materials). For all the above reasons we believed that using the periodic table as a fundamental reference would be a partly formal but easy and direct way to organize the contents of the review. Therefore, the structure of the review follows the classification of metals by groups. It is worth noting that cases in which two or more metals are involved in the same reducing system will be found in the section corresponding to the most active or key metal. Similarly, reports covering different metals or metal-containing compounds as individual reducing systems will be tackled in the corresponding sections for each metal or in the section corresponding to the most active metal.

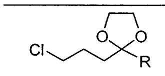
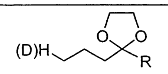
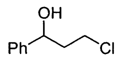
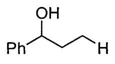
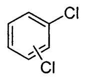
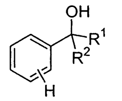
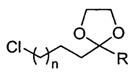
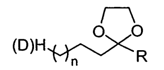
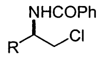
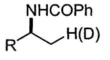
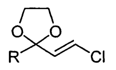
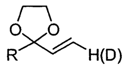
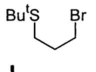
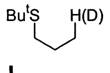
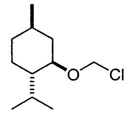
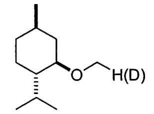
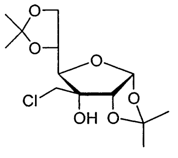
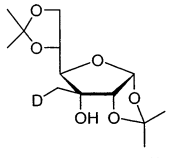
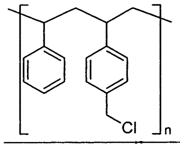
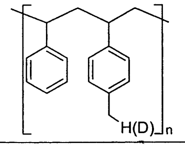
II. Alkaline and Alkaline-Earth Metals

Both alkaline and alkaline-earth metals in the zerovalent state are well-known reducing agents of the carbon−halogen bond. The reaction may involve the participation of the corresponding radical anions, species that have attracted very much attention from theoretical and synthetic points of view. For instance, the formation and decomposition reactions of halo-substituted methane derived radical anions have been investigated by the MNDO, AM1, and PM3 methods.[26a] It was observed that an increase in the number of halogen atoms, as well as a decrease in the solvent polarity, enhanced the radical anion stability, decomposition by cleavage of the carbon−hydrogen bond also being possible. The possible presence and role of intermediate radical anions in the electron-transfer reduction of organic halides has been properly reviewed, the concepts of consecutive and concerted dissociative mechanisms having been examined.[26b−g]

A. Lithium

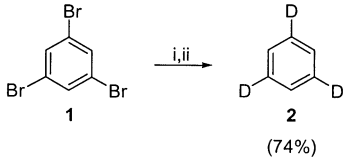
One of the simplest ways to effect the halogen−hydrogen interchange in an organic halide consists of using lithium as an electron source followed by the addition of a proton source. In the past few years, Yus et al. have developed a methodology based on the use of lithium powder and a catalytic amount of an arene, naphthalene or 4,4′-di-*tert*-butylbiphenyl (DTBB), which has been applied to the generation of very reactive organolithium intermediates under very mild reaction conditions, either from halogenated or nonhalogenated materials.[27] Thus, the lithiation reaction under these conditions (alternatively stoichiometric lithium naphthalenide was used in some cases) applied to a series of alkyl, aryl, vinyl, and benzyl chlorides or to an alkyl bromide, followed by the addition of water or deuterium oxide, led to the corresponding reduced products (Table 1).[28]

Table 1. Reduction of Organic Halides with the System Li−Arene

Starting material	Conditions	Product	Yield(%)$^{\text{ref.}}$
 R = H, Me	$LiC_{10}H_8$, -78 °C		80-90[28a,b]
	i) Bu^nLi, -78 °C ii) Li, $C_{10}H_8$ (1%)		89[28c]
	i) Li, $C_{10}H_8$ (3%), -78 °C ii) R^1COR^2		63-96[28d]
 R = H, Et, Ph n = 2, 3	Li, $C_{10}H_8$ (4-8%), -78 °C		73-92[28e,f]
 R = Et, Ph	i) Bu^nLi, -78 °C ii) $LiC_{10}H_8$		84-91[28g,h]
 R = Pr^n, Pr^i	Li, DTBB (4%), -90 °C		67-90[28i,j]
	Li, $C_{10}H_8$ (2.5%), -78 °C		80[28k]
	Li, DTBB (5%), 0 °C		67-80[28l]
	i) Bu^nLi, -78 °C ii) Li, DTBB (5%)		65[28m]
	Li, DTBB (10%), -78 °C		100[28n]

1,3,5-Trilithiobenzene was successfully synthesized by reaction of 1,3,5-tribromobenzene (**1**) with lithium−DTBB in THF at −78 °C. This lithiated intermediate when subjected to deuteriolysis with deuterated methanol furnished 1,3,5-trideuteriobenzene (**2**) in 74% yield, together with minor amounts of di- and monodeuteriobenzene (Scheme 1). The method was much more effective than the halogen−metal exchange with conventional organolithium bases, which failed in this transformation.[29]

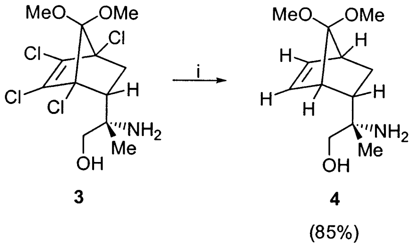
Scheme 1[a]



[a] Reagents and conditions: i, LiDTBB, THF, −75 °C; ii, MeOD.

A modification of the traditional Birch reduction conditions allowed the selective dechlorination of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene Diels−Alder adduct **3**. The key to this method is that the reductant (lithium in liquid ammonia) was added inversely to a dilute solution (10−20 mM) of **3** in ethanol at −78 °C in diethyl ether (Scheme 2).[30]

Scheme 2[a]

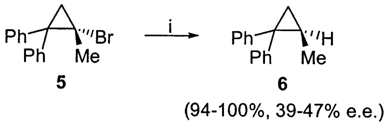


[a] Reagents and conditions: i, Li, liq NH_3, EtOH, Et_2O, −78 °C, high dilution, inverse addition.

Under normal Birch conditions, unsaturated amino alcohol **4** was obtained in only 39% yield, which suffered overreduction, leading to the corresponding saturated amino alcohol as byproduct in 20% yield (see also Scheme 10).

Walborsky et al. observed that chiral cyclopropyl bromides **5** reacted with alkali metals (lithium, sodium, or potassium), the resulting hydrocarbons **6** being optically active and with retention of configuration (Scheme 3). The best reaction yields were obtained with lithium and sodium, whereas the optical purity of the product was around 45% irrespective of the metal used. This behavior, which was rationalized in terms of a surface-bound intermediate, is in contrast with that observed when calcium was used instead of alkali metals (see below).[31]

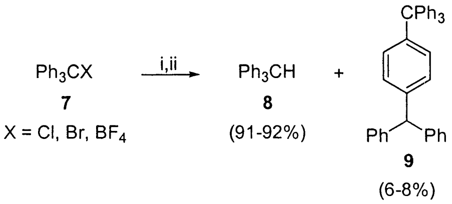
Scheme 3[a]



[a] Reagents and conditions: i, Li (or Na), ROH (R = Me, Pr^i, Bu^t).

Hindered lithium dialkylamide bases were used for the reduction of trityl derivatives **7** in THF, to give predominantly triphenylmethane (**8**) and a small amount of trityl dimer **9** (Scheme 4). A study on the reduction mechanisms revealed that the reactions are first-order in monomeric base and trityl chloride. Inter- and intramolecular kinetic isotope effects employing β-deuterium-substituted bases and substituent effect studies, coupled with other kinetic information, were used to formulate a scheme of reactions. An inner-sphere electron-transfer mechanism was considered the most likely.[32]

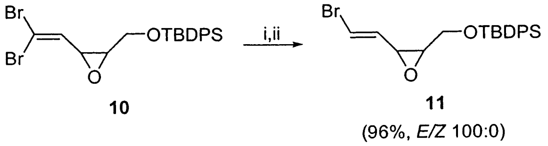
Scheme 4[a]



[a] Reagents and conditions: i, LDA or LBEA (lithium *tert*-butylethylamide), THF, −78 °C; ii, MeOH.

A series of 1,1-dibromoalkenes quantitatively yielded monobromoalkenes when treated with 1 equiv of an organolithium reagent followed by hydrolysis.[33] Dibromovinyl epoxide **10** was chosen as the model compound for the screening of reagents and conditions (Scheme 5). Methyllithium in THF at very low temperature proved to be the most selective reagent since only the (*E*)-bromovinyl epoxide **11** was detected. Bu^nLi, Bu^tLi, or PhLi, as well as the presence of LiBr, HMPA, or Et_2O (which slowed the halogen−metal exchange) instead of THF, decreased the selectivity. Substrates where the epoxide function was substituted by a cyclopropyl, cyclohexyl, or open-chain group were also studied.

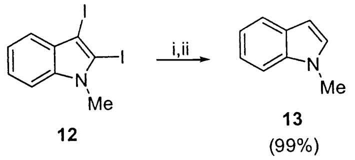
Scheme 5[a]



[a] Reagents and conditions: i, MeLi, THF, −105 °C; ii, MeOH.

Gribble et al. reported the generation of 2,3-dilithio-*N*-methylindole from 2,3-diiodo-*N*-methylindole (**12**) by treatment with *tert*-butyllithium at −78 °C in THF. The organolithium intermediate was trapped with different electrophiles, and in particular with saturated aqueous ammonium chloride, affording the complete deiodinated product *N*-methylindole (**13**) (Scheme 6).[34]

Scheme 6[a]

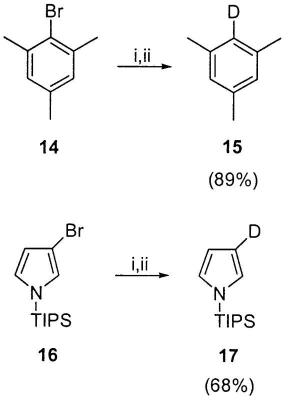


[a] Reagents and conditions: i, Bu^tLi, THF, −78 °C; ii, NH_4Cl, H_2O.

Very efficient deuteriodehalogenation was reported by Cintrat et al. involving bromine−lithium exchange, followed by treatment with 9-deuterio-9-

phenylfluorene as a deuterium donor.[35] Under these conditions, mesityl bromide (**14**) and 3-bromopyrrole derivative **16** were transformed into the corresponding labeled products **15** and **17** in fair yields and good isotopic enrichment (100% and 91%, respectively) (Scheme 7).

Scheme 7[a]



[a] Reagents and conditions: i, Bu^{n}Li, THF, −78 °C; ii, [9-^{2}H]-9-phenylfluorene.

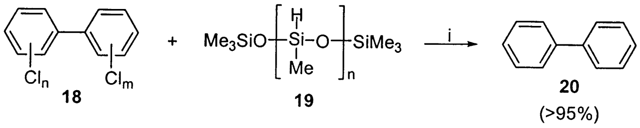
As an example of the synthetic applications of hydrodehalogenation reactions using alkyllithium reagents, regiospecific *para*-monodeiodination of 2,4-diiodophenols was achieved with Bu^{n}Li at −100 °C, this methodology being utilized in the synthesis of aflatoxin B$_2$.[36]

B. Sodium

Sodium metal has been used in a dehalogenation technique for recycling of postconsumer plastics containing halogenated compounds, used as flame retardants. Experiments were performed using various flame-retardant polystyrene master batches and polystyrene plastic waste. The technique is based on the reaction of sodium with the halogens in the plastic samples, leading to alkali-metal halides.[37] The reaction of sodium atoms with PTFE under ultrahigh-vacuum conditions, which was followed by photoelectron spectroscopy (XPS), also showed surface defluorination together with the formation of sodium fluoride.[38] A metallic sodium dispersion based process was developed by several groups to study the dechlorination and decomposition behavior of PCBs.[39,40]

Sodium metal in conjunction with a poly(methylhydrosiloxane) (PMHS), **19**, proved to be a very efficient system to achieve the complete dechlorination of a series of PCBs **18** at ambient conditions (Scheme 8).[41] Dechlorination proceeded via the formation of a polychorobiphenyl radical anion, which underwent carbon−chlorine bond cleavage with a regioselectivity similar to that normally observed in nucleophilic substitution of polyarenes. Dramatic differences were observed when the reaction was carried out in the absence of PMHS, the main difference between the two reductions being that the hydrogen abstraction step by the aromatic radical was dominant in the PMHS reduction. A regioselective stepwise dechlorination pathway was constructed on the basis of an extensive product analysis of samples during the course of the reaction, in which only 16 of the most abundant congeners of Arochlor 1254 were considered.

Scheme 8[a]

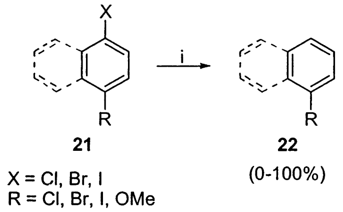


[a] Reagents and conditions: i, Na sand, THF, 2 h, rt.

Sodium in liquid ammonia was successfully applied in polymer chemistry to dehalogenate the flame retardant tetrabromobisphenol A, chemically bound to epoxy resins, carrying out the reaction in an autoclave at elevated temperatures.[42] The debromination efficiencies of solvolysis with ethyl acetate (280 °C, 15 MPa) and debromination with sodium in liquid ammonia (100 °C, 6 MPa) were compared.

Rossi et al. reported a novel and selective reagent, sodium amalgam in liquid ammonia, for the dehalogenation of aryl halides **21** (Scheme 9).[43] In general, the reaction was faster, and better yields were obtained in the presence of benzonitrile as a redox catalyst.[43a] *p*-Chloroanisole and *p*-dichlorobenzene were the only substrates which did not undergo any reduction. However, this system was very chemoselective for aryl halides containing two different halogen atoms, such as *p*-chlorobromo-, *p*-chloroiodo-, or *p*-bromoiodobenzene, the order of reactivity being the expected one.[22] 1-Chloronaphthalene yielded naphthalene quantitatively.

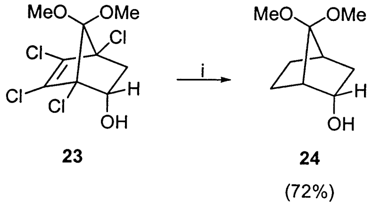
Scheme 9[a]



[a] Reagents and conditions: i, Na−Hg, liq NH$_3$, Bu^{t}OH (or PhCN).

Under similar reaction conditions, (−)-7,7-dimethoxy-1,4,5,6-tetrachlorobicyclo[2.2.1]hept-5-en-2-*endo*-ol (**23**) suffered reduction on the carbon−carbon double bond and complete dechlorination on the bicyclic skeleton (Scheme 10).[44]

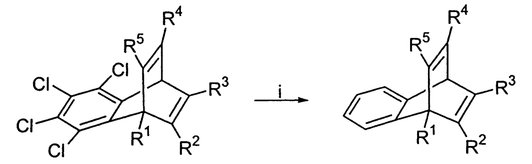
Scheme 10[a]



[a] Reagents and conditions: i, Na, liq NH$_3$, EtOH.

Tetrachlorobenzobarrelenes **25** proved to be very difficult to dehalogenate by different methods such as sodium−biphenyl−glyme, magnesium−2-propanol−decalin or potassium hydroxide−Raney nickel alloy, whereas hydrazine hydrate in the presence of palladium on charcoal led to overreduction of the olefinic bond. However, sodium and *tert*-butyl alcohol at reflux accomplished the nearly quantitative reductive dehalogenation of **25**, furnishing the corresponding benzobarrelenes **26** (Scheme 11).[45] Even the highly hindered 1,3,5-tri-*tert*-butyltetrachlorobenzobarrelene was dechlorinated using this methodology in almost quantitative yield.

Scheme 11[a]



25

26

(72-98%)

R^1 = H, Me, Bu^t, OMe, OH, NMe$_2$
R^2, R^3, R^4 = H, Me, Bu^t
R^5 = H, Me

[a] Reagents and conditions: i, Na, Bu^{t}OH, THF, reflux, 24 h.

Bunnet et al. reported the radical-induced deiodination of substituted iodobenzenes by methanolic sodium methoxide in the presence of AIBN [azobis-(isobutyronitrile)].[46] The process occurred by a radical-chain mechanism involving electron transfer to the aryl iodide as the crucial step. Mingled and separated competition experiments,[46b] using *m*-chloroiodobenzene as standard, allowed the determination of the relative reactivities of pairs of substituted iodobenzenes and the establishment of a reactivity index for each aryl iodide. The substituent effects on deiodination reactivity observed were consistent with the mechanistic model proposed.

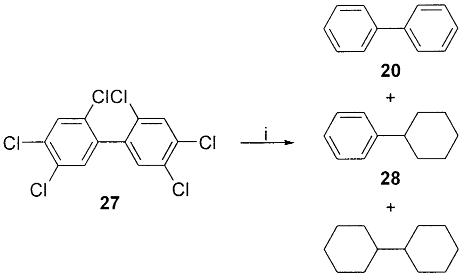
Trichloroethylene (TCE) was rapidly and completely dechlorinated by treatment with NaOH solutions at high temperatures.[47] The reaction was strongly temperature dependent: the half-lives for TCE degradation in 2 M NaOH at 40, 60, 80, and 100 °C were 347, 48.8, 4.0, and 2.4 min, respectively. The observed end products were primarily chloride anion and sodium glycolate, both of which are nonhazardous. A nucleophilic substitution of chlorine by hydroxyls was proposed as the mechanism.

It is known that commercial NaH itself is a poor reducing agent for the hydrogenolysis of organic halides. However, NaH of nanometric size, prepared catalytically by direct hydrogenation of NaH under atmospheric pressure,[48a] allowed the quantitative transformation of 1-bromonaphthalene into naphthalene, and of 1,2-dibromobenzene into benzene in refluxing THF.[48b] Other halogenated substrates such as benzyl chloride and 1,2-dichloroethane led to toluene and ethylene, respectively. The high reactivity of this NaH resides in its very small primary particle size and large specific surface area. NaH in DMSO and in the presence of sulfoxides, sulfones, and sulfolanes found application in the dechlorination of PCBs.[48c]

C. Potassium

The potassium–sodium alloy, as a modification of sodium powder as reducing agent, has been recently applied to the complete dechlorination (>99.9998%) of 2,2′,4,4′,5,5′-hexachlorobiphenyl (HCB, **27**) under an inert gas atmosphere.[49] The reaction was carried out in either benzene or cyclohexane, and although it proceeded at room temperature, the best dechlorination degree was achieved after refluxing for 2 h. Trace amounts of PCBs by stepwise dechlorination and polychlorinated quaterphenyls, as a result of the Wurtz–Fitting reaction, were detected as reaction intermediates, but completely dissappeared at the final stage. The main reaction products were biphenyl (**20**), cyclohexylbenzene (**28**), and dicyclohexyl (**29**) (Scheme 12). An estimated dechlorination pathway was proposed in which dechlorination at the *para*-position is preferred to that at the *ortho*-position.

Scheme 12[a]



27

20

28

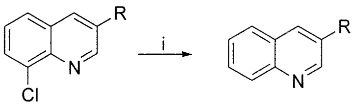
29

[a] Reagents and conditions: i, K–Na, PhH or CyH, reflux, 2 h.

Effective dehalogenation of pentachlorophenol present in wood-preserving waste was achieved with potassium poly(ethylene glycol). Greater dechlorination was observed in wastes treated at higher temperatures (80 and 120 °C). The effect of the treatment on the waste toxicity was examined, a general decrease in waste genotoxicity being observed. However, additional treatment was required for complete detoxification.[50]

The system composed of KOH–poly(ethylene glycol) (PEG) was applied by several groups to the reductive dehalogenation of organic halides. For instance, 8-chloroquinolines **30** were quantitatively dechlorinated with KOH–PEG(400) in refluxing xylene (Scheme 13).[51] Good results were also obtained for 2-iodobiphenyl (88%) and chlorodiphenylmethane (98%). However, brominated starting materials, such as 1-bromonaphthalene and 1-bromooctadecane, led to a lower yield (41%) and to the E2 elimination product, respectively.

Scheme 13[a]



30

R = H, Et

31

(100%)

[a] Reagents and conditions: i, KOH, PEG(400), xylene, reflux.

A chemical method based on KOH–PEG was also tested for the destruction of liquid PCBs. It was found that the method could be used successfully for the higher chlorinated Delor 106 from nonpolar hydrocarbon liquids, whereas di- and trichlorinated biphenyls present in Delor 103 showed low reactivity, thus preventing its efficient application in the more frequent cases of the purification of PCB-contaminated mineral oils.[52] Besides the system KOH−PEG,[53] KOH−1,3-dimethyl-2-imidazolidinone[54] or KOBu^t [55] also found application in the removal and destruction of PCBs. Potassium *tert*-butoxide in DMSO could be efficiently applied in the dehalogenation of 1,1-dichlorocyclopropanes to monochlorocyclopropanes.[56]

D. Magnesium

Egorov et al. reported the low-temperature dehalogenation of benzyl halides with atomic magnesium both in the ground state (1S)[57a] and in the 3P[57b] state. In the first case, the reaction was carried out in an HMPA matrix, following a one-electron-transfer mechanism, in which HMPA coordinates to magnesium (even at 77 K), thus stabilizing radical anion pairs and causing the reaction to proceed in part along the radical ion pathway. The formation of radical ion pairs, which is a reversible process, is accompanied by reaction of the benzyl halides with the radical ion pair ($Mg^{\bullet+}$)($HMPA^{\bullet-}$), according to the dissociative electron capture mechanism. In the second case, a radical mechanism together with abstraction of the halogen atom by the biradical Mg atom was proposed. A wide series of benzylic halides were also dehalogenated by flash vacuum pyrolysis over magnesium at 600 °C, giving rise to the corresponding bibenzyls (36−80%) and toluenes (1−28%) in good to excellent combined yields.[58]

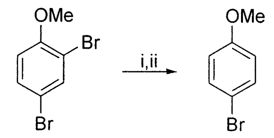
The reaction of cyclopropyl bromide with magnesium in diethyl ether yielded directly ∼30% cyclopropane. The reaction performed in perdeuterated diethyl ether and diethyl ether in the presence of the radical trap deuterated dicyclohexylphosphine confirmed that cyclopropane was formed mainly by disproportionation of the cyclopropyl radicals on the magnesium surface (∼85%), and only a small amount (∼15%) by reaction of a freely diffusing radical with the solvent.[59]

It was shown that the presence of magnesium oxide or calcium oxide allowed the destructive adsorption of chlorinated benzenes (mono-, di-, and trichlorobenzenes) at lower temperatures rather than simple pyrolysis or combustion processes.[60] Chlorine-containing products were never emitted from the MgO reactor bed, benzene along with CO, CO_2, and H_2O being the only reaction products. The carrier gases air and hydrogen led to slightly more and cleaner volatile products. MgO was compared to CaO, the former being more recommended for its higher surface area, and because it prevented the formation of small amounts of dibenzo-*p*-dioxin and monochlorodibenzo-*p*-dioxin that occurred with CaO.

Grignard reagents themselves cannot be considered good dehalogenating agents. In fact, dehalogenated products are obtained in minor amounts above all when other competing functional groups are present in the same molecule. For instance, the reaction of *o*-bromo- and *o*-iodobenzophenone with PhMgBr led to a distribution of products, the dehalogenated ones representing 16−20% of the total yield.[61] In another example, monodefluorination, together with conjugate addition, was observed in the reaction of a series of vinylic magnesium bromides with 2-(trifluoromethyl)propenoic acid.[62] However, as occurred for alkaline metals, the halogen−magnesium exchange using Grignard reagents,[63] followed by the addition of a proton source, is an alternative methodology that allows the two-step hydrodehalogenation of organic halides in a regio- and stereoselective manner in many cases.

In this context, Ohno et al. studied the reaction of various bromoanisoles with an excess of an alkyl Grignard reagent, RMgX (R = Et, Pr^i, Cy; X = Cl, Br), in THF at 40 °C, which followed by hydrolysis furnished the corresponding debrominated anisoles.[64] It is noteworthy that with polybrominated anisoles only the bromine atom *ortho* to the methoxy group was exchanged (Scheme 14).

Scheme 14[a]



32 **33** (93%)

[a] Reagents and conditions: i, Pr^{i}MgCl, THF, 40 °C, 5 h; ii, H_2O, 0 °C.

Highly regioselective monodebromination of dibromothiophene **34** was reported by Knochel et al., by treatment with Pr^{i}MgBr in THF at −40 °C, followed by hydrolysis with water. In this case, the presence of the ester function seemed to accelerate the exchange reaction (Scheme 15).[65]

Scheme 15[a]

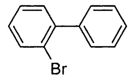
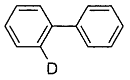
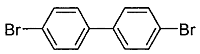
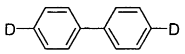
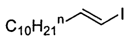
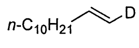
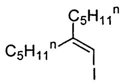
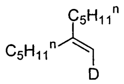
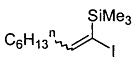
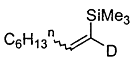
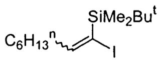
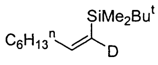
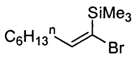
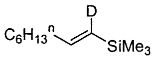
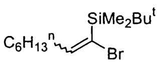
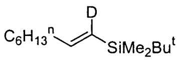
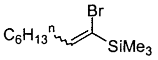
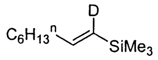
34 **35** (90%)

[a] Reagents and conditions: i, Pr^{i}MgBr, THF, −40 °C, 1 h; ii, H_2O.

Oshima et al. reported the successful halogen−magnesium exchange of a series of aryl and alkenyl halides with the magnesium ate complexes tributylmagnesate (Bu^n_3MgLi) and dibutylisopropylmagnesate (Pr^iBu_2MgLi), the latter showing higher reactivity.[66] The addition of deuterium oxide as electrophile led to the corresponding deuterated products (Table 2). Very interesting results were obtained when alkenyl iodides were subjected to iodine−magnesium exchange followed by deuteriolysis, the reaction proceeding with complete retention of the stereochemistry of the carbon−carbon double bond. However, for 1-silylalkenyl halides as starting materials, a strong preference for the bulky silyl group being *trans* to the alkyl group was observed in the reduced products.

On the other hand, the combination of Grignard reagents with transition-metal complexes has proved to be very powerful in dehalogenation reactions, and will be treated in section VI.

Table 2. Reduction of Organic Halides via Halogen−Magnesium Exchange

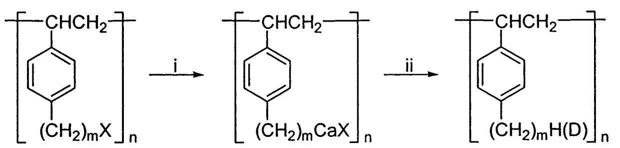
Starting material	Conditions	Product	Yield(%)
	i, Bu$^n{}_3$MgLi, THF, 0 °C ii, D$_2$O		93
	i, Bu$^n{}_3$MgLi, THF, 0 °C ii, D$_2$O		100
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		93
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		87
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		98
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		89
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		90
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		86
	i, Pr^{i}Bu$_2$MgLi, THF, 0 °C ii, D$_2$O		99

E. Calcium

Mechanochemical processes using Ca, CaO, or CaH$_2$ have been applied by several groups to the very effective dechlorination of different chlorinated materials. Thus, CaO was the preferred reactant, in comparison with Mg, Ca, or Fe, in the dechlorination of DDT, PCBs (Arochlor 1254), and chlorobenzene, the reaction occurring at low temperature in a sealed environment and leading to safe reaction products.[67] Cocco et al. studied the dehalogenation of hexachlorobenzene and chlorobenzene by mechanical treatment with CaH$_2$, using a ball milling process at low temperature and atmospheric pressure.[68a] A dechlorination degree of up to 100% was achieved, the products being practically restricted to benzene and calcium chloride. The use of CaH$_2$ as a source of active hydrogen produced a much more specific reaction in significantly less time in comparison with the reaction with CaO and MgO under a hydrogen atmosphere. A similar technique was applied to the reduction of the herbicide 2-(2,4-dichlorophenoxy)-propionic acid.[68b]

Rieke et al. discovered that highly reactive calcium could be obtained by reduction of calcium halides with preformed lithium biphenylide in THF.[69a] This calcium readily reacted with lightly cross-linked polystyrene resins **36** containing chloromethyl, bromine, chlorine, and fluorine moieties to prepare functionalized polymers **37** in excellent yields. The addition of water or deuterium oxide as electrophile led to the hydrodehalogenated polymers **38** in quantitative yield (Scheme 16).[69b]

Scheme 16[a]



36 **37** **38**

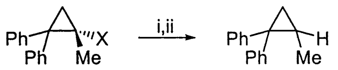
X = F, Cl, Br; m = 0
X = Cl; m = 1

(100%)

[a] Reagents and conditions: i, active Ca, THF, rt; ii, H$_2$O or D$_2$O.

The above methodology was extended by Walborsky et al. to the reduction of (*S*)-1-halo-1-methyl-2,2-diphenylcyclopropanes **39**, which after rapid quenching with dilute hydrochloric acid yielded completely racemic 1-methyl-2,2-diphenylcyclopropane (**6**) (Scheme 17).[70] On the basis of this observation, the formation of the organocalcium compounds was believed to occur via electron transfer rather than halogen−metal exchange, therefore providing free radicals in solution as intermediates.

Scheme 17[a]



39 **6**

X = Cl, Br (45-100%, 0% e.e.)

[a] Reagents and conditions: i, active Ca, THF, −20 °C, 0.5 h; ii, 10% HCl.

III. Group IIIA Metals

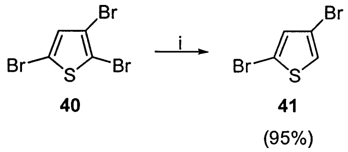
The major part of this section will deal with the application to the reduction of organic halides of the nucleophilic reducing agents lithium aluminum hydride (LAH) and sodium borohydride and their corresponding derivatives.[21,25c,d] Reactions of these hydrides induced or catalyzed by transition metals will be studied in section VI.

A. Boron

The reductive chemistry of sodium borohydride[71] was compared with that exhibited by other hydride reagents through implementation in the CAMEO program.[72] A series of levels of the reactivity of functional groups were established, in which the reactivity decreases with increasing level number, and functional groups belonging to a lower level selectively undergo reduction in the presence of functional groups belonging to higher levels. Organic halides were covered in this computer-assisted study, showing levels of reactivity of 1 (acyl chlorides), 4 (alkyl or aryl bromides and iodides), and 6 (alkyl or aryl chlorides) within a scale from 1 to 6. In comparison, with LAH, levels of 1 (acyl chlorides) and 2 (alkyl or aryl chlorides, bromides, and iodides) within a scale from 1 to 3 were shown. These results are consistent with the milder reactivity and better selectivity of NaBH$_4$ as reducing agent.

Sodium borohydride was utilized for the regioselective debromination of 2,3,5-tribromothiophene (**40**) in DMSO at room temperature to furnish 2,4-dibromothiophene (**41**) in 95% yield (Scheme 18).[73] On the other hand, catalytic amounts of Pd(Ph_3P)$_4$ led mainly to 2,3-dibromothiophene, other nickel or palladium catalysts producing considerable amounts of 3-bromothiophene (see section VI).

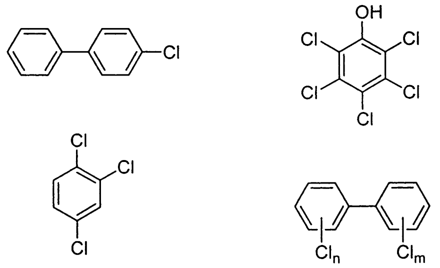
Scheme 18[a]



[a] Reagents and conditions: i, $NaBH_4$, DMSO, 26 °C, 4 h.

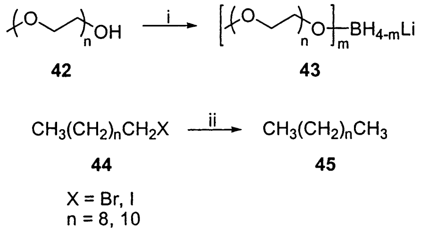
Pittman et al. have developed a method for the effective dechlorination of different chlorinated materials based on the use of $NaBH_4$ in high boiling point glyme solvents (Chart 1). In a preliminary study,[74a] 4-chlorobiphenyl was completely dechlorinated to biphenyl with $NaBH_4$ in tetraglyme at 310 °C in 1 h. However, the addition of LiCl to $NaBH_4$ promoted dechlorination at 120−135 °C in di-, tri-, and tetraglyme, an enhancement in the rate of the reaction being observed when $NaBH_4$, LiCl, and glyme were prestirred at room temperature for 20 min before being heated to 120−135 °C. Under equivalent conditions, dechlorination rates followed the order tetraglyme > triglyme > diglyme, the reaction failing when diphenyl ether was used instead of these solvents. Under the same optimized reaction conditions, pentachlorophenol and 1,2,4-trichlorobenzene were also dechlorinated, the latter requiring stronger thermal treatment (300 °C, 2 h).[74b] More recently, the system $NaBH_4$−LiCl−glyme at 125−135 °C effected the quantitative dechlorination of PCB Arochlor 1016, the dechlorination rates following the pattern mentioned above. 2-Chlorobiphenyl and 2,2′-dichlorobiphenyl were the least reactive congeners with $NaBH_4$−LiCl in diglyme, a competitive dechlorination also being observed in which 3-chloro- and 4-chlorobiphenyl reacted faster than 2-chlorobiphenyl at 130 °C.[74c,d]

Chart 1. Compounds Dechlorinated with $NaBH_4$−LiCl−Glyme at 120−300 °C



A series of borohydride−poly(ethylene glycol) monomethyl ether (borohydride−PEGMME) derivatives were prepared by allowing low molecular weight PEG **42** (M_w = 350) to react with $LiBH_4$, $NaBH_4$, or KBH_4. The chemoselectivity of these derivatives was studied, $LiBH_4$−PEGMME (**43**) being the most active and the least selective, and finding application in the reduction of alkyl halides **44** at 25 °C (Scheme 19).[75]

Scheme 19[a]

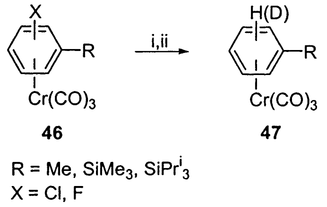


[a] Reagents and conditions: i, $LiBH_4$, PhMe, 85 °C, 2 h; ii, **43**, PhMe, 25 and 85 °C.

Lithium aminoborohydrides emerged as a new class of powerful but selective reducing agents able to reproduce, in air, virtually all the transformations for which lithium aluminum hydride is normally used. Among them, lithium pyrrolidinoborohydride allowed the effective reduction of alkyl halides such as 1-iododecane and benzyl bromide to the corresponding alkanes in excellent yields, 92% and 95%, respectively.[76]

Superhydrides Et_3BHLi and Et_3BDLi reacted with *ortho*-halogenated (X = Cl, F) toluenetricarbonylchromium and trialkylsilylbenzenetricarbonylchromium complexes **46**, giving rise to the corresponding hydrodehalogenated products **47** (Scheme 20).[77] Deuteride was observed to add preferentially at the *meta*-position to the leaving group in the case of the silylated complexes via a *tele-meta* nucleophilic aromatic substitution.

Scheme 20[a]



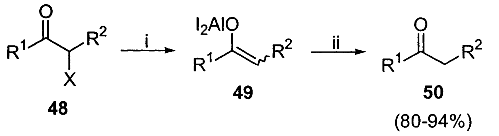
[a] Reagents and conditions: i, Et_3BHLi (or Et_3BDLi), THF (rt or −78 °C), 1−3 h; ii, CF_3CO_2H.

B. Aluminum

About a decade ago Sandhu et al. reported the utility of aluminum triiodide as a mild and selective reagent for the efficient reductive dehalogenation of α-halocarbonyl compounds **48** via generation of an aluminum enolate intermediate, **49**.[78] This reagent was successfully applied to both linear and cyclic α-haloketones and to α-haloamides, the carbon−halogen bond in aromatic substituents suffering no cleavage (Scheme 21).

It was recently reported that Al−Hg promoted the chemoselective reductive cleavage of the carbon−halogen bond of α-halocarboxylates, allowing a facile and clean transformation of halohydrin aldol adducts **51** into β-hydroxy acid derivatives **52** with no evidence of dehydroxyhalogenation (Scheme 22).[79] The reaction proceeded under very mild reaction conditions, with excellent yields and in short reaction times, even in the presence of groups which are

Scheme 21[a]

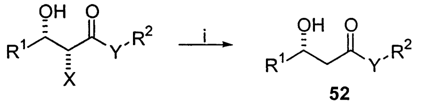


48 **49** **50** (80-94%)

R^1 = Ph, p-XC_6H_4, PhNH, p-XC_6H_4NH
R^2 = H, Ph
X = Cl, Br

[a] Reagents and conditions: i, AlI_3, MeCN, 80 °C; ii, H_2O.

Scheme 22[a]



51 **52** (20-96%)

R^1 = Pr^i, (E)-prop-1-enyl, Ph
R^2 = Me, Bu^t, allyl, Bn, PMB
X = Cl, Br, I
Y = O, NH

[a] Reagents and conditions: i, Al−Hg, MeCN−H_2O, 0−25 °C, 2−60 min.

particularly prone to hydrogenolysis. Good results were also obtained when the substrate was an amide instead of an ester.

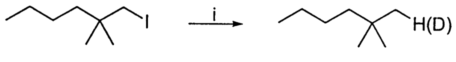
Alumina was used as a support in the hydrodehalogenation reaction of different types of organic halides. For instance, bromochlorodifluoromethane (Halon 1211, $CBrClF_2$) was thermally hydrodehalogenated using a plug flow alumina reactor at atmospheric pressure over the temperature range 400−900 °C, with residence times of 2−4 s and with $CBrClF_2$:hydrogen molar intake ratios of ca. 10.[80] Conversion of $CBrClF_2$ started at ca. 400 °C with carbon−bromine bond cleavage followed by reaction with HX (X = Br, Cl, H) to yield $CHClF_2$. Complete conversion of $CBrClF_2$ was achieved at 600 °C, and complete dehalogenation to mainly methane (80%) was attained above 850 °C. Alternatively, methane could be used instead of hydrogen for the above transformation, elevated temperatures causing the replacement of the product $CHClF_2$ by $C_2H_2F_2$.[81]

An alumina support was also involved in the dechlorination of octachlorodibenzo-p-dioxin and octachlorodibenzofuran.[82] The acidity of the alumina was an important parameter to take into account in the dechlorination of these compounds. Alkaline alumina showed better behavior than acidic alumina. Metal chlorides were less effective in comparison with alumina, and an electrophilic substitution mechanism was suggested in the latter case.

The reduction of alkyl halides to the corresponding hydrocarbons by LAH is a well-known reaction but nonetheless is very controversial from the mechanistic point of view. Newcomb on one hand and Ashby on the other hand have dedicated many efforts to find some evidence concerning this reaction mechanism. Of remarkable importance should be considered the contributions to this field by Ashby et al. during the past decade.

In one of the preliminary studies, Ashby et al. presented strong support that the reaction of secondary alkyl iodides and hindered primary alkyl iodides with LAH proceeded to a significant extent by a single-electron-transfer process (SET), an S_N2 mechanism being considered as a minor pathway.[83a] A detailed mechanism of the SET nature of the reaction was proposed by using radical probes, in which a radical-chain process in addition to a halogen atom transfer process was suggested. However, no evidence was found that an SET was involved in the reactions of alkyl chlorides and bromides, unless a catalyst was used to initiate the reaction to produce $AlH_3^{\bullet -}$. Further work, not involving cyclizable radical probes, showed that the reaction of LAH with hindered alkyl iodides also proceeded predominantly by an SET process.[83b−d] Thus, 1-iodo-2,2-dimethylhexane (**53**) was allowed to react with $LiAlD_4$ (LAD) to furnish 2,2-dimethylhexane (**54**) with a deuterium content of 4−76%, depending on the reaction conditions, these data therefore being consistent with the participation of a radical intermediate (Scheme 23). The effect of the reactor surface was also studied. The same type of experiment with LAD extended to the saturated primary[83e] and secondary[83f] alkyl iodides 1-iodooctane and 2-iodooctane produced octane with a deuterium incorporation of 62% and 8%, respectively. An unsaturated tertiary alkyl iodide[83f] was also studied, all cases with convincing evidence that the reactions took place through an SET mechanism.

Scheme 23[a]

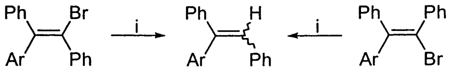


53 **54** (4-76% D)

[a] Reagents and conditions: i, LAD, THF, rt, 1−48 h.

Similar conclusions were presented by Rappoport et al. from the hydrodehalogenation of the triarylvinyl bromides (E)- and (Z)-**55**. A 54:46 E/Z mixture of the reduced product **56** was obtained in both cases, with an electron-transfer process being the most likely (Scheme 24).[84]

Scheme 24[a]



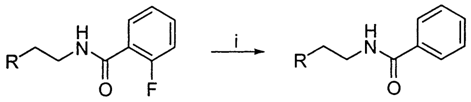
(E)-**55** **56** (Z)-**55**

Ar = β-anisyl (E/Z 54:46)

[a] Reagents and conditions: i, LAH, THF, rt.

A series of o-fluorobenzamides **57** were reduced with LAH under mild reaction conditions to give the corresponding dehalogenated products **58** in a chemospecific manner and with moderate yields (Scheme 25).[85] Chemo- and regioselective *ortho*-dehalogenation (F, Cl) was also observed when the aromatic ring also bore halogens (F, Cl) on the *meta*- or *para*-positions. A mechanism in which aluminum species stabilized by chelation with the amine nitrogen of the side chain was proposed. LAH also found application in the reductive dehalogenation, in a stream of oxygen, of heteroaromatic halides such as bromonarwedine ketone acetal or 2-bromothiophene (99% conversion to thiophene in 2−3 h).[86]

Scheme 25[a]



57 **58**

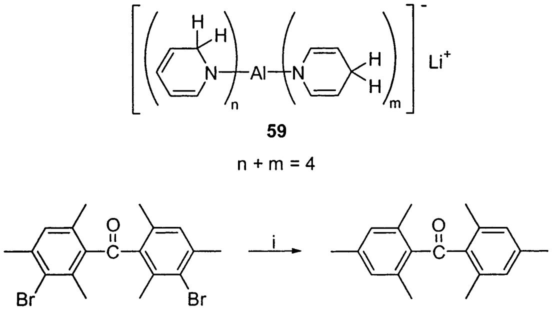
(59-78%)

R = *N*-morpholino, *N*-piperidinyl, NMe_2

[a] Reagents and conditions: i, LAH, THF, 25 °C.

LAH-derived complexes also found application as reducing agents of organic halides. For instance, it is known that a pyridine solution of LAH forms the 1:4 molecular complex lithium tetrakis(*N*-dihydropyridyl)aluminate (LDPA, **59**). This reagent proved to promote the reduction of alkyl halides by two competitive processes: hydride transfer and SET. Although the dominant pathway involved hydride transfer, a more plausible electron-transfer process took place in the reduction of the hindered 3,3′-dibromo-2,2′,4,4′,6,6′-hexamethylbenzophenone (**60**), where the hydride-transfer pathway appeared to be sterically blocked by the interaction with the bulky LDPA (Scheme 26).[87]

Scheme 26[a]



59

n + m = 4

60 **61**

(99%)

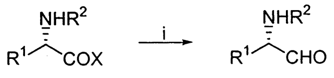
[a] Reagents and conditions: i, LDPA (**59**), THF, 61 °C, 22 h.

A powerful reducing agent, comparable to LAH, is a 1:1 LAH−*N*-methylpyrrolidine complex (LAH−NMP), obtained by reaction of LAH with *N*-methylpyrrolidine. This complex was able to reduce a wide range of functional groups, among them organic halides. 1-Bromooctane, 1-iododecane, benzyl chloride, and benzyl bromide were reduced by LAH−NMP in THF at 0 °C for 12 h, leading quantitatively to the corresponding hydrocarbons.[88]

A large variety of *N*-protected α-amino aldehydes, **63**, were readily prepared in moderate yields from the corresponding acid chlorides and fluorides **62** by reduction with lithium tris(*tert*-butoxy)aluminum hydride, the original absolute stereochemistry apparently not being compromised (Scheme 27).[89]

Vcelak et al. reported the dehalogenation of different chlorinated arenes with sodium dihydridobis(2-methoxyethoxy)aluminate (SDMA), which in many cases was studied from a kinetically and mechanistic point of view.[90] Thus, the dehalogenation of a series of mono- to pentachlorinated benzenes with SDMA was found to be first-order in the substrate and half order in the hydride. It was also observed that the reactivities of chlorobenzenes increased with increasing number of chlorine atoms over 3 orders of magnitude. This study also provided further support for the assumption that the dehalogenation with SDMA proceeded as a nucleophilic aromatic substitution, in which formation of the reaction intermediate was the rate-determining step of the reaction. The isomer distribution and rate data analysis made it possible to propose a detailed reaction sequence.[90a] This reagent also found application in the reduction of 4,4′-dichlorobiphenyl to biphenyl in toluene at 70−110 °C.[90b] In this case, the reaction course was described by two consecutive dehalogenation steps of first-order in the substrate. An acceleration in the reaction was observed in the presence of catalytic amounts of cobalt(II) and nickel(II) 1,3-pentanedionates (see section VI).

Scheme 27[a]



62 **63**

(*ca.* 60%)

R^1 = Me, Pr^i, Bu^i, Bn, $MeSCH_2CH_2$, 3-indolylmethyl
R^2 = Fmoc, Boc, Z
X = F, Cl

[a] Reagents and conditions: i, $LiAlH(OBu^t)_3$, THF, −70 °C.

C. Gallium

Choi et al. carried out a systematic study on the reduction with lithium gallium hydride (LGH) of a series of organic compounds containing representative functional groups to establish its reducing ability.[91a] Among the different substrates studied, alkyl halides, such as *n*-butyl chloride, bromide, and iodide and benzyl chloride, were rapidly reduced to the corresponding hydrocarbons with an uptake of 1 equiv of hydride. Furthermore, aromatic halides appeared to be reduced even more readily than aliphatic ones, whereas acid chlorides were converted into alcohols. It was concluded that the reactivity of LGH lies somewhere between those of the analogous aluminum and boron hydrides.[91b] The reported reactivity was decreased by transformation of LGH into the complex gallane−trimethylamine ($GaH_3 \cdot NMe_3$), able to reduce acid chlorides to alcohols but not alkyl halides.[91c] The reduction of a wide range of organic halides and differently functionalized organic halides with sodium and potassium gallium hydrides was also studied (Table 3).[91d] An analysis of the results obtained concluded that the reducing ability of $NaGaH_4$ was superior to that of $KGaH_4$. The organic halides were reduced in the expected order I > Br > Cl. In the case of aliphatic haloesters, higher selectivity was observed for 3-haloesters than for 2-haloesters. Haloaliphatic nitriles were reduced better than haloaromatic nitriles. Mingled experiments showed the selective dehalogenation of alkyl halides with $KGaH_4$ in the presence of aromatic or cyclic halides, esters, or nitriles.

α-Bromoketones **64**, treated with in situ prepared gallium triiodide or methyl gallium iodide, led to the corresponding gallium enolates **65**, which by subsequent addition of water as electrophile furnished the

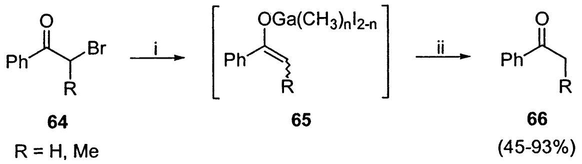
Table 3. Reduction of Organic Halides with $NaGaH_4$ and $KGaH_4$[91d]

halide[a]	X = Cl[b]	X = Br[b]	X = I[b]
$CH_3(CH_2)_6CH_2X$	95 (82)		
$CH_3CHX(CH_2)_5CH_2X$		98 (98)	
$CH_3(CH_2)_2CHX(CH_2)_3CH_3$		100 (99)	
CyX[c]	13 (tr)[d]	94 (32)	99 (45)
BnX	100 (98)	100 (100)	
PhX	7 (tr)	94 (34)	99 (99)
p-XC_6H_4Me	tr (tr)	84 (26)	96 (38)
p-XC_6H_4OMe	tr (tr)	83 (22)	97 (34)
CH_3CHXCO_2Et	(7)	(28)	
$XCH_2CH_2CO_2Et$	(63)	(91)	
p-$XC_6H_4CO_2Et$		(tr)	(14)
CH_3CHXCH_2CN		(79)	
$X(CH_2)_3CN$		(82)	
p-XC_6H_4CN		(19)	
$XCH_2C_6H_4CN$		(90)	
α-bromobutyrolactone		(99)	

[a] Reaction performed in refluxing THF. [b] GLC yield for $NaGaH_4$. GLC yield for $KGaH_4$ in parentheses. [c] Cy = cyclohexyl. [d] tr = trace.

expected debrominated ketones **66** in moderate to excellent yields (Scheme 28).[92]

Scheme 28[a]



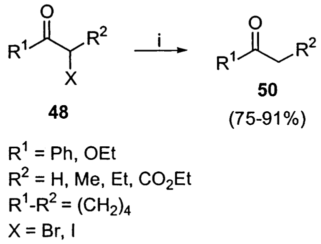
[a] Reagents and conditions: i, $(CH_3)_nGaI_{3-n}$ (n = 0−2), THF, DMF, rt.

D. Indium

During the past decade, indium has emerged as a metal of high potential in organic synthesis due to certain unique properties that it possesses.[93] Of particular interest is the reactivity of indium metal in aqueous media, including the reduction of carbon−halogen bonds, very little explored until a few years ago. For instance, in a study on indium as reducing agent, it was observed that 2-chloroquinoline was completely reduced to 1,2,3,4-tetrahydroquinoline in 79% yield by indium metal in aqueous ethanol.[94] It is also known that organoindium intermediates derived from α-haloketones undergo reduction to the corresponding ketones by proton abstraction as a lateral reaction, thus competing with other desired processes.[95]

A first systematic study on the dehalogenating power of indium was carried out by Ranu et al. This group provided an efficient and general methodology for the chemoselective reduction of α-halocarbonyl compounds and benzyl halides by indium metal in water under sonication.[96a] A wide range of structurally different α-iodo- and α-bromoketones and esters **48** underwent reduction, leading to the corresponding dehalogenated carbonyl compounds **50** (Scheme 29). Brominated substrates were reduced slower than iodinated substrates. In fact, alkyl and aryl iodides remained inert although benzyl iodides and β-iodoketones were reduced. Selective deiodination was observed at the benzylic position vs the aromatic carbon−iodine bond in the same substrate. The use of indium metal in aqueous medium was extended to the stereoselective reduction of aryl-substituted *gem*-dibromides to vinyl bromides.[96b] The reaction was performed in ethanol and saturated ammonium chloride solution under reflux, providing primarily the corresponding (*E*)-vinyl bromides (50:50 to 95:5 *E*/*Z* ratio) in high yields (70−95%). The compatibility with several sensitive functional groups (OMe, OBz, Cl, OTBDMS, and *o*-allyl) and the absence of overreduction processes are the main advantages of this methodology. However, thiophene- and furan-substituted *gem*-dibromides did not show any stereoselectivity, whereas low effectiveness was observed for alkyl-substituted *gem*-dibromides.

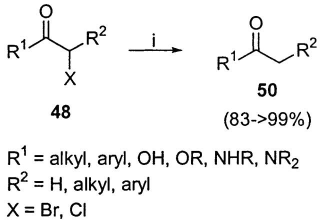
Scheme 29[a]



[a] Reagents and conditions: i, In, H_2O, ultrasound.

The use of micellar solutions as reaction media has shown an enhancement in the reactivity of certain processes.[97] Such is the case of the indium-mediated dehalogenation of α-halocarbonyl compounds **48** in water and in the presence of a catalytic amount of the surfactant sodium dodecyl sulfate (SDS).[98a] These conditions were applied by Kim et al. to α-haloketones, esters, carboxylic acids, amides, and nitriles (Scheme 30). For α-chlorocarbonyl compounds, the reaction was rather slow in comparison with that of the bromo derivatives, and a slightly higher temperature was required. In the absence of SDS, the reaction proceeded slowly and most of the starting materials were recovered unaltered after prolonged reaction times. The same group reported the efficient reductive conversion of 3-iodomethylcephalosporin into the corresponding 3-methylcephems by indium in an aqueous system.[98b]

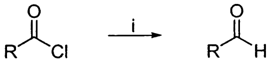
Scheme 30[a]



[a] Reagents and conditions: i, In, H_2O, 0.01 M SDS, rt to 80 °C.

Dichloroindium hydride (Cl_2InH) was recently generated by Baba et al. using the transmetalation between indium trichloride and tributylstannane at −78 °C. This new hydride was shown to be considerably stable at ambient temperature due to coordination to THF and found application in the reduction of alkyl and acid halides. Alkyl bromides, such as benzyl bromide and 1-bromo-3-phenylpropane, were readily reduced to toluene (99%) and 1-phenylpropane (77%), respectively.[99a] However, the starting material was completely recovered when the reaction was performed in toluene or in the presence of the radical inhibitors galvinoxyl or *p*-dinitrobenzene, thus indicating the radical character of the hydride. More recently, some other organic halides such as 1-bromododecane, 2-bromododecane, 1-bromoadamantane, 5-bromo-1-phenylpentanone, iodobenzene, and 1-(4-iodophenyl)-1-ethanone were effectively reduced by this system (61−91%).[99b] On the other hand, aryl and vinyl bromides and alkyl chlorides remained practically unaltered. This methodology was extended to the transformation of acid chlorides **67** into the corresponding aldehydes **68** (Scheme 31).[99c] The best results were obtained by in situ generation of the indium hydride from catalytic amounts of indium trichloride and triphenylphosphine, and stoichiometric amounts of tri-*n*-butylstannane in toluene. The reduction was successfully accomplished for a variety of acid halides, being compatible with reducible substituents such as cyano, nitro, and terminal alkene and chloride. It was believed that coordination of the phosphine improved the reducing ability of the indium hydride, a catalytic cycle being proposed for the reaction.

Scheme 31[a]



67 **68**

(39-97%)

R = Ph, *p*-MeOC$_6$H$_4$, *p*-MeC$_6$H$_4$, *p*-ClC$_6$H$_4$, *p*-CNC$_6$H$_4$, *p*-NO$_2$C$_6$H$_4$, *n*-C$_6$H$_{13}$, Cl(CH$_2$)$_5$, CH$_2$=CH(CH$_2$)$_8$, Bu^{n}CHEt, *c*-C$_6$H$_{11}$, Bu^t

[a] Reagents and conditions: i, InCl$_3$ (10 mol %), Ph$_3$P (20 mol %), Bu$_3$SnH, PhMe, −30 °C, 2 h.

IV. Group IVA Metals

Most of this section is dedicated to the application of hydrides derived from the group IVA metals to the hydrodehalogenation of organic halides under radical conditions.

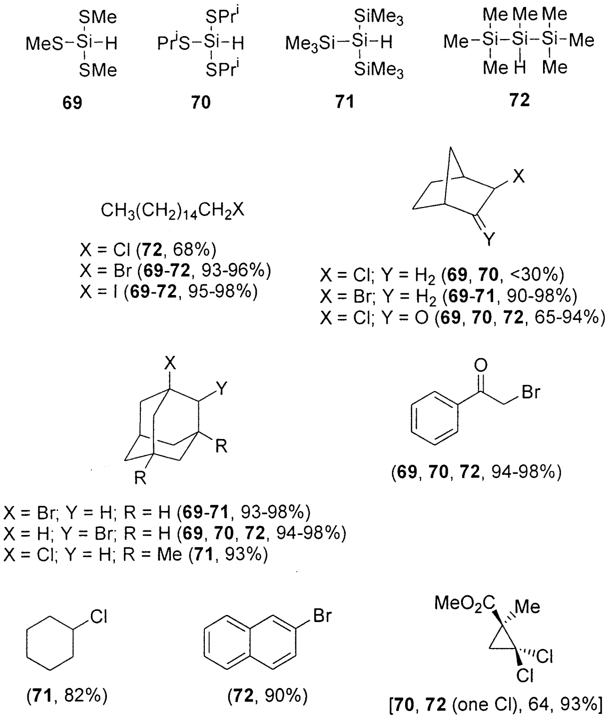
A. Silicon

Organosilicon chemistry[100] is one of the most powerful tools in synthetic organic chemistry that found wide application in the reduction of organic halides, especially with the use of silicon hydrides. Thus, organosilicon hydrides with various structures were used, in the presence of aluminum trichloride, as hydride ion donors in the ionic hydrogenolysis of alkyl halides. Triethylsilane, dimethyl(ethyl)silane, and *n*-butylsilane reduced any type of alkyl halide. Silicon hydrides with two bulky substituents such as phenyl and cyclohexyl attached to the silicon atom were only effective for alkyl halides capable of forming, in the presence of aluminum trichloride, stabilized carbenium ions such as tertiary carbenium ions or secondary and primary carbenium ions conjugated with a benzene ring.[101a] 1,1,2,2,3,3,4,4-Octaphenyltetrasilane with catalytic amounts of aluminum trichloride also furnished the expected hydrocarbons with high yields. A method was developed for the hydrogenolysis of alkyl halides in a heterogeneous medium with a column filled with a mixture of octaphenyltetrasilane and aluminum chloride, in which the silane was regenerated by reduction with lithium aluminum hydride.[101b]

Silyl radicals play a strategic role in diverse areas of science and in particular in organic chemistry, where as reducing agents they were shown to be highly efficient and superior reagents from both ecological and practical perspectives with respect to those employed before. The high reactivity of silyl radicals toward organic halides is well known, the reactivity trends having been determined from kinetic data and being the following: (a) for a particular RX, the rate constant decreased along the series Et$_3$Si$^\bullet$ > Ph$_2$Si$^\bullet$Bu^t ≈ Ph$_3$Si$^\bullet$ > Me$_3$SiSi$^\bullet$Me$_2$ > (Me$_3$Si)$_3$Si$^\bullet$; (b) for a particular silyl radical and R group, the rate constant decreased along the series X = I > Br > Cl > F; (c) for a particular silyl radical and X atom, the rate constant decreased along the series R = benzyl > *tert*-alkyl > *sec*-alkyl > primary alkyl > phenyl.[102]

The reducing abilities of organosilanes were extensively studied by Chatgilialoglu et al. This group discovered tris(alkylthio)silanes as new reducing radical agents.[103a,b] Tris(methylthio)silane (**69**) and tris(isopropylthio)silane (**70**) were applied to the reduction of a variety of organic substrates in the presence of a radical initiator (AIBN) (Chart 2). Alkyl bromides and iodides were straightforwardly and completely reduced in a short time (ca. 0.5 h). Longer reaction times and periodic addition of initiator were necessary for alkyl chlorides, whereas α-stabilized chlorides of *gem*-dichlorides were more easily dehalogenated. Evidence for a free radical mechanism was

Chart 2. Reduction of Organic Halides with Silicon Hydrides 69−72, PhMe, and AIBN (3−10 mol %) at 75−90 °C for 0.5−2 h

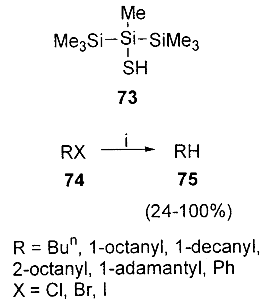


provided by the observations that the reactions were catalyzed by light and by thermal sources of free radicals such as AIBN or dibenzoyl peroxide. Furthermore, the reactions were retarded by 2,6-di-*tert*-butyl-4-methylphenol and duroquinone, which are radical inhibitors. Similar results were obtained for the radical-based reducing agents tris(trimethylsilyl)silane[103c,d] (**71**) and 1,1,1,2,3,3,3-heptamethyltrisilane (**72**) (Chart 2).[103e]

Saturated primary, secondary, and tertiary alkyl halides RX (X = Cl, Br, I) were reduced to the corresponding alkanes RH, in essentially quantitative yield, by triethylsilane in refluxing hexane (1 h) or cyclohexane in the presence of di-*tert*-butyl hyponitrite as initiator, and *tert*-dodecanethiol (mixture of isomers) as polarity reversal catalyst,[104a] which mediated hydrogen atom transfer from the Si−H group of the silane to the alkyl radical R$^\bullet$. Triphenylsilanethiol and perfluorohexanesulfenyl chloride were also effective catalysts. This silane−thiol couple allowed the effective reduction of 1-bromo-, 1-chloro, and 1-iodooctane (not for 1-fluorooctane), 2-bromooctane, 1-bromoadamantane, and 1-bromo-1-methylcyclohexane (91−99% yield). In the absence of either the thiol or the initiator, a <10% yield was obtained.[104b]

Heptamethyltrisilane-2-thiol (**73**) mediated the free-radical-chain reduction of organic halides **74**, by combining the halogen-abstracting ability of the silyl radical and the good hydrogen donor character of the thiol moiety, through a rearrangement from a thiol radical to a silyl radical.[105] The reaction was initiated by thermal decomposition of di-*tert*-butyl hyponitrite and took place with very good yields for alkyl chlorides and bromides (75−100%). Aryl halides such as iodobenzene were reduced quantitatively, whereas bromobenzene yielded only 24% benzene (Scheme 32).

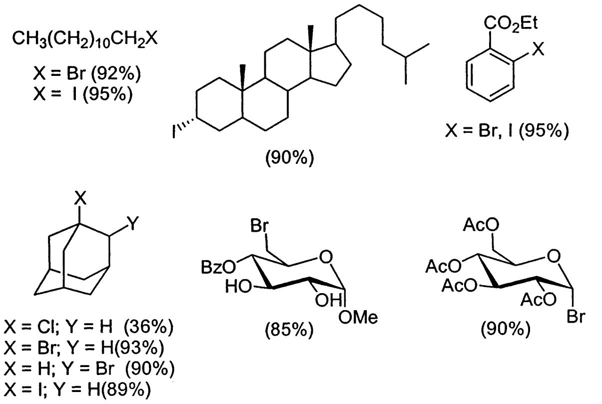
Scheme 32[a]



[a] Reagents and conditions: i, **73**, Bu^{t}ONNOBu^t (3 mol %), 80 °C.

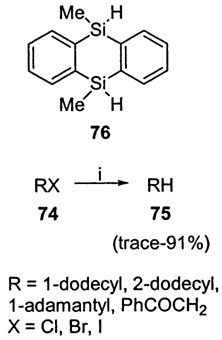
Arylsilanes were also found to be appropriate reducing agents for the radical dehalogenation of organic halides. For instance, diphenylsilane reduced 1-haloadamantanes to adamantane in refluxing toluene and in the presence of catalytic amounts of benzoyl peroxide. The best result was obtained for 1-bromoadamantane (91%), 1-chloro- and 1-iodoadamantane showing low dehalogenation degrees (8% and 35%, respectively).[106a] Better behavior was observed for reactions performed in boiling phenylsilane with AIBN as radical initiator. Excellent yields were obtained for structurally different organic halides (X = Br, I) with this methodology, including linear alkyl, cyclic, aryl, and steroid- or carbohydrate-derived halides (Chart 3).[106b]

Chart 3. Reduction of Organic Halides with Boiling $PhSiH_3$ and AIBN (0.3−1 equiv) for 70−150 min



Nishiyama et al. reported the preparation of a series of 9,10-dihydro-9-sila-10-heteroanthracenes as new radical-based reducing agents.[107] Derivatives possessing a silicon, tin, oxygen, or sulfur atom at the 10-position exhibited enhanced reactivities compared to the open-chain models. Among them, 9,10-dimethyl-9,10-dihydro-9,10-disilaanthracene (**76**) proved to be the most effective reagent for AIBN-initiated dehalogenation of organic halides **74**. The reactivity of this compound was found to be comparable to that of tris(trimethylsilyl)silane, and was especially effective in the reduction of primary, secondary, and tertiary bromides and α-bromoketones (81−91%). Chlorinated substrates were more reluctant to dehalogenate (trace to 5%) probably due to the significant decrease in the rate of chlorine abstraction by the silyl radical (Scheme 33).

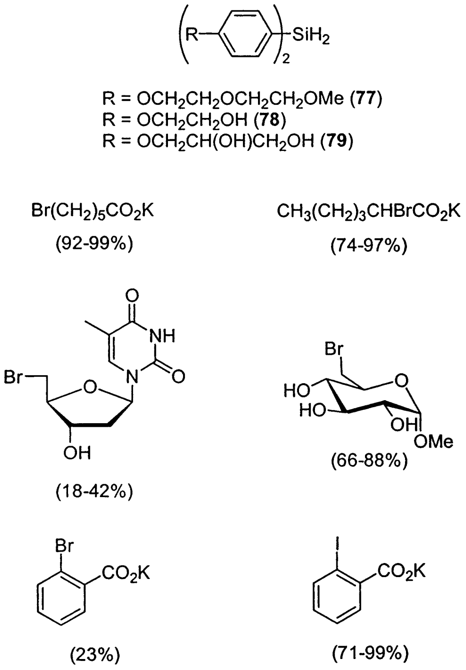
Scheme 33[a]



[a] Reagents and conditions: i, **76**, AIBN, 80 °C.

Arylsilanes as radical reducing agents were widely studied by Togo and Yokoyama et al.[108] This group synthesized a series of organosilane compounds, the reactivity of which was studied in the radical reduction of 2-bromoethyl phenyl ether (as model compound), initiated by triethylborane in ethanol under aerobic conditions at room temperature. The results obtained showed that arylsilanes were more reactive than alkylsilanes. In addition, the reactivity of diarylsilanes was superior to that of monoarylsilanes and triarylsilanes. For instance, diphenylsilane was the most efficient reagent for the reduction of 2-bromoethyl phenyl ether to phenetole (73%) under the above-mentioned reaction conditions. From this point, several water-soluble diarylsilanes, **77**−**79**, were developed to promote the radical reduction of alkyl and aryl bromides and iodides, initiated by triethylborane, in aqueous media under aerobic conditions. This methodology was very useful for the reduction of water-soluble substrates such as halocarboxylates and halosugars (Chart 4).[108a]

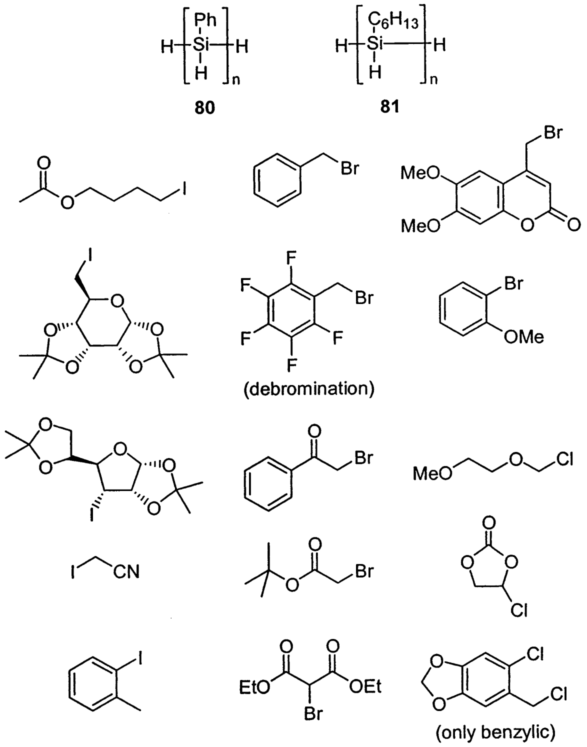
Chart 4. Reduction of Organic Halides with Diarylsilanes 77−79, Et_3B, and H_2O at rt



This research group also studied the reactivity of 1,1,2,2-tetraphenyldisilane as a radical reagent in the reduction of several alkyl bromides in ethanol promoted by AIBN or triethylborane. The results obtained indicated that one or two hydrogen atoms bonded to silicon in $Ph_4Si_2H_2$ participate in the reaction; therefore, more than 1 equiv of the silane was necessary to obtain the reduction product in good yield. The following substrates were reduced in moderate to excellent yields: 2-bromoethyl phenyl ether (97%), 6-bromo-6-deoxy-α-D-glucopyranoside (97%), cholestanyl bromide (99%), 5′-bromo-5′-deoxythimidine (35%), and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (68%). A considerable difference between $Ph_4Si_2H_2$ and Ph_2SiH_2 was observed, the latter reaching only a 3% yield in the reduction of 2-bromoethyl phenyl ether.[108b,c]

Polysilanes of the type $H(RSiH)_nH$ where R = Ph (**80**) or *n*-hexyl (**81**) also found application as radical-based reducing agents for organic halides.[109] The repetitive hydrogen transfer from the same molecule of polysilane allowed these compounds to be used in small quantities. The photochemical behavior of these polysilanes in the presence or absence of di-*tert*-butyl peroxide was studied by EPR spectroscopy, the $-SiHR-Si^{\bullet}R-SiHR-$ radical (R = *n*-hexyl) being identified as a transient species. A large variety of organic chlorides, bromides, and iodides were successfully hydrodehalogenated with yields higher than 86% (Chart 5). Evidence of a free radical mechanism was provided by the observation that the reactions started only in the presence of radical initiators were retarded by 2,6-di-*tert*-butyl-4-methylphenol or duroquinone, and were inhibited by nitroxides such as TEMPO.

Chart 5. Reduction of Organic Halides with Polysilanes 80 and 81 and AIBN at 82−85 °C for 1−3 h (86−100%)

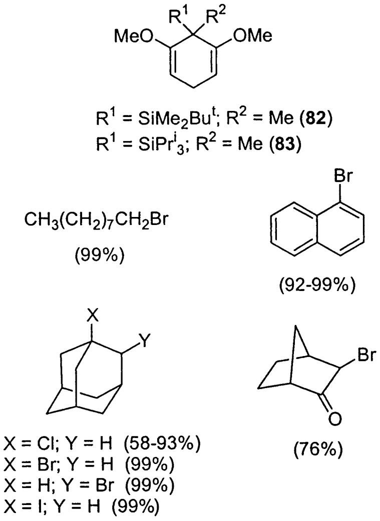


More recently, Studer et al. prepared silylated cyclohexadienes **82** and **83** from resorcinol dimethyl ether by Birch reduction and subsequent one-pot silylation−methylation. These compounds combine the hydrogen donor ability of 1,4-cyclohexadienes with the ease to propagate radical-chain processes by halogen abstraction of the silyl radical moiety. The reduction of various halogenated substrates was carried out with AIBN in refluxing hexane, affording the expected dehalogenated products in most cases with yields higher than 92% (Chart 6).[110] Alternatively, the reduction of bromoadamantane was conducted very well under an atmosphere of air, without using an initiator, to give adamantane in almost quantitative yield.

B. Germanium

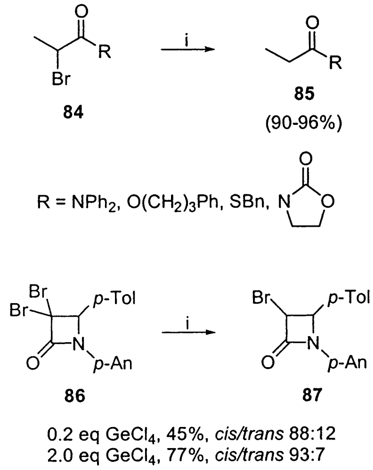
The triphenylphosphine−germanium(IV) chloride combination was found to be effective for the dehalogenation of various α-bromo carboxylic acid derivatives **84**.[111] It was believed that the activation of the carbon−halogen bond in α-halocarbonyl compounds, upon coordination of a Lewis acid to their carbonyl oxygen, would compensate the rather low reducing power of triphenylphosphine. The reaction was carried out with catalytic amounts of germanium(IV)

Chart 6. Reduction of Organic Halides with Silylated Cyclohexadienes 82 and 83 and AIBN in Refluxing Hexane



chloride in the presence of water at room temperature. Under these optimized conditions, examples of α-bromo amide, ester, thioester, and imide were reduced in high yields (Scheme 34). The selective half-reduction of the α,α-dibromo-β-lactam **86** was also achieved; however, 2 equiv of $GeCl_4$ was recommended to improve both the yield and the diastereoselectivity.

Scheme 34[a]



R = NPh_2, $O(CH_2)_3Ph$, SBn,

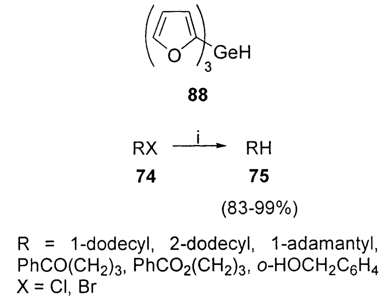
0.2 eq $GeCl_4$, 45%, *cis/trans* 88:12
2.0 eq $GeCl_4$, 77%, *cis/trans* 93:7

[a] Reagents and conditions: i, Ph_3P (2 equiv), $GeCl_4$ (0.2 equiv), H_2O (1 equiv), THF, rt or reflux.

Germanium hydrides have attracted the attention of different groups due to their ability as hydrogen donors in radical reactions. In this context, it was reported that tri-*n*-butylgermanium hydride was an effective hydrogen-transfer agent for perfluoro-*n*-alkenyl radicals.[112] In comparison with other hydrides, it was observed that Bu^n_3GeH has virtually the same reactivity as $(Me_3Si)_2SiMeH$ and a lower reactivity than $(Me_3Si)_3SiH$. Kinetic studies on a variety of germanium hydrides were also performed by Chatgilialoglu et al. to determine the hydrogen donor power toward primary alkyl radicals.[113] The results of this study revealed an increase in the rate constant along the series $Bu^n_3GeH < Ph_3GeH < (Me_3Si)_3GeH$. For a particular substituent on the hydride, the rate constant followed the order $R_3SiH < R_3GeH < R_3SnH$. Finally, for a particular metal hydride the rate constant increased along the substituent series alkyl < phenyl < Me_3Si. The stability of the $(Me_3Si)_3Ge^\bullet$ radical was rationalized in terms of hyperconjugation between the bonding and/or antibonding Si−C β-bond.

The germanium hydride tri-2-furylgermane (**88**) was utilized in the triethylborane-induced radical reduction of organic halides **74** in good yields and under mild reaction conditions (Scheme 35).[114] A catalytic version of this reaction in the presence of sodium borohydride was also examined and applied to primary (1-iodododecane and 1-bromododecane), secondary (2-bromododecane), and tertiary (1-bromoadamantane) halides in good yields (73−98%). Functional groups such as ester or tetrahydropyranyloxy survived under the reaction conditions, whereas the alkyl chloride 1-chlorododecane was recovered almost unchanged.

Scheme 35[a]

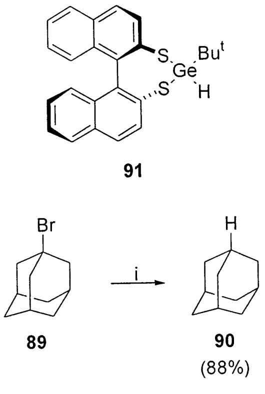


R = 1-dodecyl, 2-dodecyl, 1-adamantyl, $PhCO(CH_2)_3$, $PhCO_2(CH_2)_3$, *o*-$HOCH_2C_6H_4$
X = Cl, Br

[a] Reagents and conditions: i, **88**, Et_3B, THF, rt.

In a report on the synthesis and asymmetric hydrogermylation reactions of dithiogermanium hydrides, Curran et al. demonstrated that *rac*-**91** moderates radical-chain reductions by accomplishing hydrodebromination of 1-bromoadamantane (**89**) in the presence of AIBN (Scheme 36).[115]

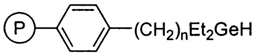
Scheme 36[a]



[a] Reagents and conditions: i, *rac*-**91**, AIBN, PhH, 80 °C.

Polystyrene-supported[116] organogermanium hydrides **92**−**94** were prepared by functionalization of a polystyrene or by functionalization of a styrene followed by polymerization (Chart 7). These hydrides were capable of reducing organic halides by heating with free radical initiators, no coupling

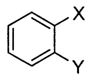
Chart 7. Reduction of Organic Halides with Polymer-Supported Organogermanium Hydrides 92−94 and Bu^tOOBu^t at 135 °C for 2 h



n = 0 (**92**), 1 (**93**), 2 (**94**)

$CH_3(CH_2)_6CH_2X$

X = Cl (**92**, 10%), (**93**, trace), (**94**, 34%)
X = Br (**92**, 17%), (**93**, 20%), (**94**, 60%)
X = I (**92**, 54%), (**93**, 45%), (**94**, 60%)



X = Cl; Y = H (**92**, 0%), (**93**, 0%), (**94**, trace)
X = Br; Y = H (**92**, 13%), (**93**, trace), (**94**, 45%)
X = I ; Y = H (**92**, 38%), (**93**, 44%), (**94**, 55%)
X = Cl; Y = Br (**92**, 4%), (**93**, 13%), (**94**, 22%)
X = Br; Y = Br (**92**, 7%), (**93**, 10%), (**94**, 40%)

products being detected.[117] The observed order of reactivity was **94** > **93** > **92**, because of the decrease in the steric crowding around the germanium atoms as the number of methylene groups was increased. The reactivity of the halogen atoms following the sequence I > Br > Cl and that of the substituents in the order RX > PhX were those expected according to the homolytic reduction of organic halides with trialkylgermyl hydrides previously reported. Polyhalobenzenes *o*-bromochlorobenzene and *o*-dibromobenzene were reduced stepwise to afford chlorobenzene and bromobenzene, respectively.

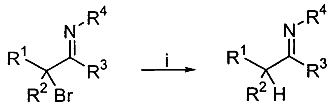
C. Tin

Metallic tin or zinc was used to direct crossed aldol-type condensations in aqueous media between α-halocarbonyl compounds and aldehydes. In many cases, the reduced product coming from dehalogenation of the α-halocarbonyl compound was obtained as a byproduct. For instance, in the reaction of 2-bromo-2-methyl-1-phenylpropan-1-one with benzaldehyde and tin at 70 °C, the aldol product was formed together with the reduction product, whereas at 85 °C only the reduced product was quantitatively generated.[118]

A new reducing system composed of magnesium−tin(II) chloride dihydrate was developed for the chemoselective reduction of aldehydes into alcohols, also being able to dehalogenate benzyl halides such as benzyl chloride, bromide, and iodide to toluene in 90% yield.[119] It is worthy to note that the anhydrous metal salt and metal in anhydrous tetrahydrofuran did not react, even after long exposure. However, addition of a few drops of water initiated a vigorous exothermic reaction with evolution of hydrogen and formation of metallic tin particles, which started the reductive dehalogenation.

More recently, De Kimpe et al. described a new method for the efficient hydrodebromination of α-bromo imines **95** using tin(II) chloride in methanol at ambient temperature. Aliphatic ketimines, aromatic ketimines, and aldimines were subjected to these reaction conditions to furnish the hydrodebrominated products **96** in good to excellent yields (85−96%) (Scheme 37).[120] Taking advantage of the fact that α-chloro imines were not affected by this reagent, an α-bromo-α-chloro ketimine was chemoselectively transformed into the corresponding α-chloro imine in 90% yield.

Scheme 37[a]



95 **96**
(85-96%)

R^1 = Me, Bu^t, Cl, Br
R^2 = H, Me, Et
R^3 = H, Me, Pr^i, Ph, *p*-ClC_6H_4
R^4 = Pr^i, Bu^t, Cy

[a] Reagents and conditions: i, $SnCl_2$ (1.5−3.0 equiv), MeOH, rt.

Organotin hydrides are certainly the most used organotin compounds in the laboratory, which have proved to be capable and versatile for both radical generation and kinetically controlled radical trapping.[121a−c] By far, the most used tin hydride is tri-*n*-butyltin hydride (TBTH), with applications in many fields of synthesis including the replacement of halogen by hydrogen. The reduction of an alkyl halide by TBTH can be considered the most commonly employed indirect technique to determine the kinetics of an alkyl radical reaction.[121d] The rate constants obtained by this method allow one to know at what concentrations a radical precursor will be reactive enough to propagate a good chain reaction and to anticipate whether an atom- or group-transfer reaction will be faster or slower than other possible competing reactions.

In a seminal investigation, Curran et al. determined the rate constants for halogen abstraction by tributyltin radical from a representative series of aryl and vinyl bromides and iodides.[122] Relatively high reactivity was observed for aryl bromides and iodides, the latter being equalled as radical precursors only by reactive precursors such as alkyl bromides, and exceeded only by alkyl iodides. Variations in reactivity within the series of aryl and vinyl bromides studied were rather small, the general trend being rationalized in terms of polar effects for aryl bromides (4-bromoanisole < 4-bromoacetophenone < 4-bromobenzonitrile) or by using standard arguments for vinyl bromides [primary vinyl < secondary vinyl, cyclic secondary vinyl < acyclic (*Z*)-alkene, or (*Z*)-alkene < (*E*)-alkene].

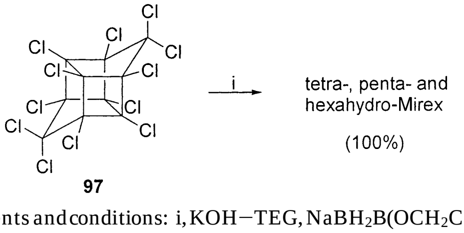
Dolbier et al. measured the absolute rate constants for the abstraction of hydrogen of perfluoro-*n*-alkyl radicals from TBTH in solution at room temperature.[123a] The higher reactivity of perfluoro-*n*-alkyl radicals in comparison with *n*-alkyl radicals was attributed to the high electrophilicities of the former. The radical $C_2F_5^•$ was somewhat more reactive than *n*-$C_3F_7^•$, *n*-$C_7F_{15}^•$, and *n*-$C_8F_{17}^•$, these three radicals exhibiting essentially equal reactivities. The rates of hydrogen transfer to perfluoro-*n*-alkyl radicals and *n*-alkyl radicals by TBTH were also compared to the ones obtained for silane reducing agents and thiophenol, an important enhancement in the rate being observed for the silanes.[123b]

The dehalogenation reaction of organic halides (RX) by tri-*n*-butyltin radical has been extended to a wide variety of substrates, for which bond dissociation values of the carbon−halogen bond undergoing homolysis were obtained from thermochemical cycles, and correlated with the energy of activation values.[124] The rates of dehalogenation in benzene at 80 °C showed the following trends: (a) holding the R group constant, the iodides were more reactive than bromides, which in turn were more reactive than chlorides; (b) within the same halide series, the benzoyl and alkyl derivatives were more reactive than the aryl and vinyl compounds; (c) aromatic positional isomers did not differ significantly in reactivity, and the effect of substituents was not pronounced. These experimental findings appear to be bound to the different strengths of the carbon−halogen bonds: the stronger the bond, the slower the halogen abstraction process. They also confirm the view that the dehalogenation of the substrate by tri-*n*-butyltin radical represents the rate-determining step of the process.

The system TBTH−AIBN is by far the most utilized for radical-promoted hydrodehalogenation of organic halides. For instance, in the early 1990s Lin et al. applied it to the efficient dechlorination of 2′-chloro-3′-*O*-imidazolycarbonyl and 2′-chloro-3′-*O*-acetyl nucleosides to give the corresponding 2′-deoxynucleosides in 97% and 96% yield, respectively.[125]

We have already remarked in section II on the reducing properties of the system KOH−PEG. Either this system or KOH−tetraethylene glycol (TEG), when used in combination with sodium borohydride or alkoxyborohydrides, led to a very powerful reducing medium which quantitatively destroyed Mirex (**97**). Di-, tri-, and tetrahydro-Mirex (60−100%) were obtained with KOH−TEG−$NaBH_4$, the reaction being accelerated by the presence of TBTH−AIBN (18 h). However, the best results were obtained when Mirex was treated with KOH−TEG and an alkoxyborohydride with catalytic amounts of TBTH−AIBN, with complete transformation of the pesticide into tetra-, penta-, and hexahydro-Mirex in 1 h at 58 °C (Scheme 38).[126]

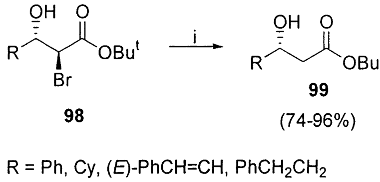
Scheme 38[a]



[a] Reagents and conditions: i, KOH−TEG, $NaBH_2B(OCH_2CH_2OMe)$, $Bu^n{}_3SnH$, AIBN, 58 °C, 1 h.

anti-α-Bromo *β*-hydroxy esters **98**, which were synthesized by Corey et al., are useful precursors of acetate aldols **99**, obtained in good yields by debromination with TBTH−AIBN in refluxing benzene or toluene. In general, shorter reaction times and better yields were observed with toluene in comparison with benzene (Scheme 39).[127]

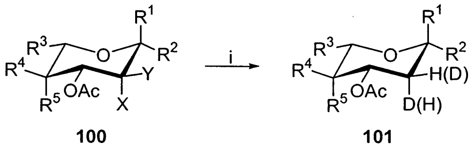
Scheme 39[a]



[a] Reagents and conditions: i, $Bu^n{}_3SnH$, AIBN, PhH or PhMe, reflux, 30 min to 15 h.

The stereochemistry of dehalogenation of a range of 2-halosugars **100** with TBTH was investigated in terms of the influence of steric and conformational effects using deuterium-labeling techniques (Scheme 40).[128] The radical character of the process was evidenced since methyl glycoside derivatives having different halogen substituents and/or configurations at C-2 underwent dehalogenation with $Bu^n{}_3SnD$ to give the isomeric monodeuterated products in the same axial:equatorial ratio (Table 4, entries 1−3).

Scheme 40[a]

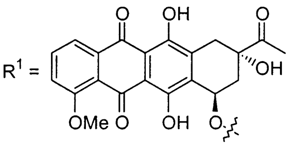


[a] Reagents and conditions: i, $Bu^n{}_3SnD$, AIBN, PhH, 60 °C, 1 h.

Table 4. Dehalogenation of 2-Halosugars 100 with Tri-*n*-butyltin Deuteride

entry	X	Y	R^1	R^2	R^3	R^4	R^5	ax:eq
1	I	H	OMe	H	Me	OAc	H	80:20
2	Br	H	OMe	H	Me	OAc	H	80:20
3	H	Br	OMe	H	Me	OAc	H	80:20
4	I	H	OPr^i	H	Me	OAc	H	90:10
5	Br	H	OPr^i	H	Me	OAc	H	90:10
6	I	H	OBu^t	H	Me	OAc	H	95:5
7	I	H	a	H	Me	OAc	H	100:0
8	H	I	H	OMe	Me	OAc	H	60:40
9	H	Br	H	OMe	Me	OAc	H	60:40
10	H	I	H	OPr^i	Me	OAc	H	60:40
11	H	Br	H	OPr^i	Me	OAc	H	60:40
12	H	I	H	OBu^t	Me	OAc	H	60:40
13	I	H	OMe	H	Me	OAc	H	80:20
14	I	H	OMe	H	H	OAc	H	75:25
15	H	I	H	OMe	Me	OAc	H	60:40
16	H	I	H	OMe	H	OAc	H	40:60
17	I	H	OMe	H	Me	H	OAc	50:50
18	I	H	OMe	H	H	H	OAc	35:65
19	H	I	H	OMe	Me	H	OAc	10:90
20	H	I	H	OMe	H	H	OAc	0:100

[a]



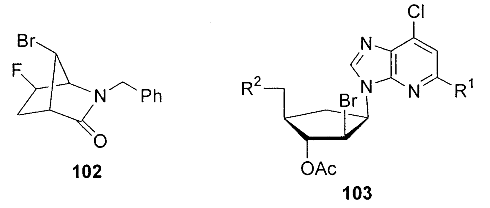
The proportion of axially deuterium-labeled product increased with the steric bulk of the aglycon. When the aglycon lay in the equatorial disposition, the proportion of axial vs equatorial epimers remained the same (60:40), despite the size of the group (Table 4, entries 8−12). Steric effects were also evident when the orientation of the 4-*O*-acetyl group changed from equatorial to axial (compare entries 13 and 17, 14 and 18, 15 and 19, and 16 and 20 in Table 4). When the 5-methyl group was replaced by hydrogen, an increase of the equatorially labeled isomer was observed (compare entries 13 and 14, 15 and 16, 17 and 18, and 19 and 20). To explain this behavior, a rapid interconversion between radical conformers was proposed, undergoing competitive reduction from the axial and equatorial directions.

TBTH proved to be an effective reagent for the debromination of 2-bromonaphthoquinones though dechlorination proceeded only with 30% yield. Good results were also obtained with the zinc−silver couple for the debromination reaction, but dechlorination only occurred in traces and did not occur at all with triethylsilane.[129]

A series of polyhalofluorocarbons, including $CF_3(CF_2)_5I$, $H(CF_2)_4CH_2I$, $CF_3CF_2CH_2I$, $HCF_2CF_2CH_2I$, $ICH_2(CF_2)_3CH_2I$, $ClCF_2CFClCF_2Cl$, $ClCF_2CFClCFClCF_2Cl$, $ClCF_2CFClCF_2CFCl_2$, and $Cl_2CFCF_2CF_2CF_2CFCl_2$, and nonfluorinated materials such as *cis*- and *trans*-1,2-dichlorocyclobutane and *cis*- and *trans*-1,2-dichlorocyclopentane were reduced with TBTH to afford the corresponding hydrofluorocarbons (HFCs) and hydrodechlorinated products, respectively, in good to excellent yields (67−98%).[130] TBTH led, in general, to better yields in comparison with other reducing agents such as zinc or LAH. In some cases, no radical initiators were required, neat TBTH inducing an exothermic reaction that could be maintained at 100 °C by controlling the rate of addition.

Roberts et al. used the TBTH−AIBN system to selectively hydrodebrominate the 2-azabicyclo[2.2.1]heptan-3-one derivative **102**[131a] and the carbocyclic nucleosides **103**,[131b] in the presence of fluorine and chlorine, respectively (Chart 8).

Chart 8. Compounds Hydrodebrominated with Bu^n_3SnH and AIBN in PhH at Reflux (68−92%)



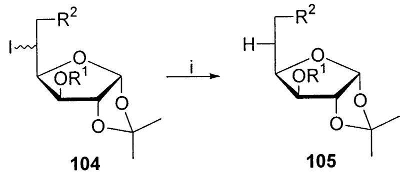
102

103

R^1 = NH_2, Cl
R^2 = CH_2OAc, CH_2OH, $CH(OAc)CH_2OAc$

In a similar way, diastereomeric mixtures of 5-iodo compounds **104**, bearing perfluorinated substituents, were hydrodeiodinated by treatment with TBTH−AIBN in moderate yields to form the corresponding 5-deoxy products **105** (Scheme 41).[132]

Scheme 41[a]



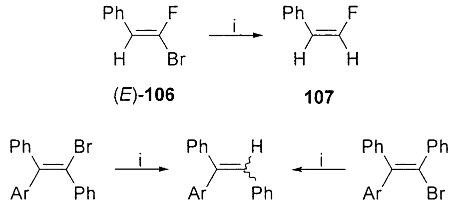
104 **105**

R^1 = Me, Bn
R^2 = C_6F_{13}, C_8F_{17}

[a] Reagents and conditions: i, Bu^n_3SnH, AIBN, PhMe, 60 °C, 6−8 h.

In a study on the effect of substituents on the structure of α-substituted vinyl radicals, Rappoport et al. described the hydrodebromination of pure (*E*)-**106** with TBTH−AIBN in refluxing benzene, giving the single product *cis*-*β*-fluorostyrene (**107**) (Scheme 42).[133] The reaction was suggested to take place through the corresponding bent α-fluorovinyl radical with retention of configuration, and supported by the results of calculations. However, under these reaction conditions, the stereochemical behavior of the α-phenylvinyl radical intermediate derived from either (*E*)- or (*Z*)-**55**, which was calculated to be linear, demonstrated loss of configuration, as happened with LAH (see Scheme 24).[84]

Scheme 42[a]



(*E*)-**106** **107**

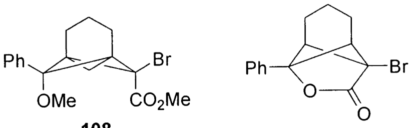
(*E*)-**55** **56** (*Z*)-**55**

Ar = β-anisyl (*E/Z* 55:45)

[a] Reagents and conditions: i, Bu^n_3SnH, AIBN, PhH, reflux.

Razin et al., in a study on the synthesis of substituted bicyclo[3.1.1]heptanes, utilized TBTH for the stereospecific hydrodebromination of **108** and hydrodebromination of **109** (Chart 9).[134]

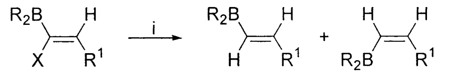
Chart 9. Compounds Hydrodebrominated with Bu^n_3SnH and AIBN



108 **109**

The reaction of (*Z*)-1-halo-1-alkenyldialkylboranes **110** with TBTH at 0 °C or room temperature resulted in the reductive removal of the halogen atom to furnish (*E*)- or (*Z*)-1-alkenyldialkylboranes **111** and **112**, respectively (Scheme 43).[135] The stereochemistry of the products was found to be dependent on the dialkylboryl group and the alkenyl moiety in **110**, and was explained in terms of either radical or ate complex formation processes. Thus, the percentage of (*Z*)-isomer increased with an increase of the bulkiness of the dialkylboryl group or the presence of a phenyl group in the alkene unit. It is worth noting that, in general, the stereoselectivity was

Scheme 43[a]



110 **111** **112**

R = Cy, siamyl, thexyl; R^1 = Bu^n, Bu^t; X = Br; **111/112** >99:<1-<1:>99
R = Cy, siamyl, thexyl; R^1 = Ph; X = Br, I; **111/112** 31:69-1:99

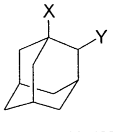
[a] Reagents and conditions: i, Bu^n_3SnH, THF (air), 0 °C or rt, 1 h.

notably improved when the reaction was carried out in the presence of a small amount of air.

The diethylzinc−air system was useful for the initiation of tin-mediated radical reactions of organic halides. Primary, secondary, and tertiary bromides and iodides were reduced to the corresponding alkanes (Chart 10).[136] The presence of air dramatically enhanced the yield of the dehalogenated products, in general, and as expected, the chain propagation of alkyl iodides was more efficient than that of alkyl bromides.

Chart 10. Reduction of Organic Halides with Bu^n_3SnH, Et_2Zn (5 mol %), and PhH or PhMe in the Air at 20 (−78) °C for 1 h

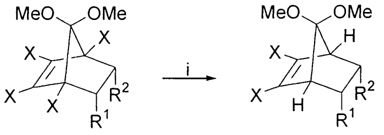
n-$C_{12}H_{25}Br$ (96%)
n-$C_8H_{17}I$ (100%)
n-$C_6H_{13}CH(CH_3)I$ (93%)



X = Br; Y = H (97%)
X = H; Y = Br (90%)
X = I; Y = H (94%)

Khan et al. developed a simple and preparatively useful TBTH-mediated selective bridgehead hydrodehalogenation of tetrahalonorbornene derivatives **113**.[137] The methodology was applied with success to a series of tetrachloro- and tetrabromonorbornenes, the reduction not affecting the vinylic halogens. A wide range of functional groups were compatible with these reaction conditions (Scheme 44).

Scheme 44[a]



113 **114**

(65-97%)

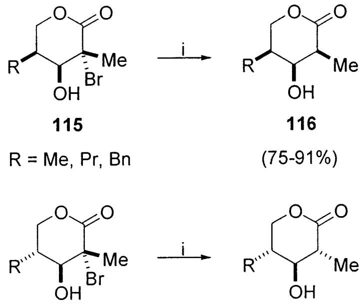
$R^1 = R^2 = CO_2Me$, CH_2OH
R^1-R^2 = CON(Ph)CO, COOCO
R^1 = H; R^2 = CN, CO_2Me, Ph, CH_2OH
X = Cl, Br

[a] Reagents and conditions: i, Bu^n_3SnH, AIBN, PhH, reflux, 1.5−60 h.

Reduction of organic halides catalytic in tin was reported by Maleczka et al., in which PMHS,[138] in combination with potassium fluoride, was used to regenerate the tin hydride.[139] It was assumed that the active species in this reaction were hypervalent silane species, although the presence of highly coordinated organotin species was not ruled out. The standard reaction conditions were 10−20 mol % tributyltin chloride, PMHS, aqueous potassium fluoride, AIBN, and refluxing toluene. Under these conditions 1-chloro-1,1-diphenylmethane, ethyl α-bromoacetate, and *o*-iodoanisol were hydrodehalogenated in 45%, 95%, and 96% yield, respectively.

An interesting 2,4-*syn*-dialkyl diastereoselection has been recently observed in the radical debromination of α-bromo-α-methyl-*δ*-valerolactones **115** and **117** (Scheme 45).[140] The distinctive 2,4-*syn* selection appeared to be affected only by the chiral center at C-4, completely independent of the direction of the hydroxy function at C-3. The stereochemical outcome was rationalized on the basis of the avoidance of steric hindrance between the substituent at C-4 and the incoming TBTH, the latter approaching the radical center at C-2 from the opposite side. On the other hand, low 2,4-*syn* diastereoselection was observed in the radical debromination of *γ*-lactones.

Scheme 45[a]



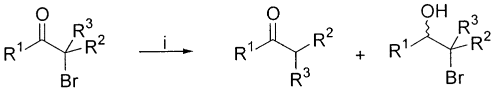
115 **116**
R = Me, Pr, Bn (75-91%)

117 **118**
R = Me, Pr, Bn (66-76%)

[a] Reagents and conditions: i, Bu^n_3SnH, Et_3B, PhMe, −78 °C, 2 h.

Tin hydrides, structurally different from TBTH, have also been applied to the reduction of organic halides. For instance, it is known that di-*n*-butyltin dihydride exhibits higher reducing ability than TBTH, and it was used in the chemoselective reduction of α-bromoketones **119**.[141] Without any additive, di-*n*-butyltin dihydride acted as an efficient debrominating agent to afford the corresponding ketones **120**, whereas the addition of small amounts of a radical inhibitor, such as *p*-dinitrobenzene, resulted in carbonyl group reduction to provide the corresponding bromohydrin **121** (Scheme 46). *p*-Nitrophenacyl bromide was reduced at the carbonyl group even in the absence of additive due to the fact that the *p*-nitro group itself acts as a radical inhibitor.

Scheme 46[a]



119 **120** **121**

(30-91%)

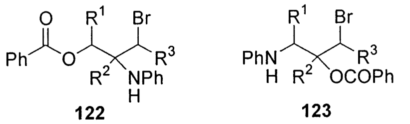
120/**121** 82:18-100:0

R^1 = Me, Ph, p-$MeOC_6H_4$, p-ClC_6H_4
R^2 = H, Me, Et, Bu^n
R^3 = H, Me

[a] Reagents and conditions: i, $Bu^n_2SnH_2$ (0.5 equiv), 0 °C, 3 h.

Very efficient hydrodebromination of compounds **122** and **123** with triphenyltin hydride (TPTH) and AIBN was reported by Engman, giving rise to the expected amino alcohol derivatives (Chart 11).[142]

Chart 11. Compounds Hydrodebrominated with Ph_3SnH, AIBN, and PhH at Reflux for 2 h

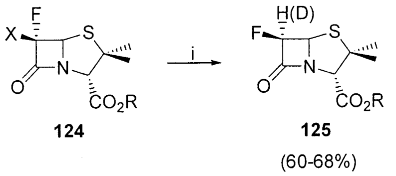


122 **123**

R^1, R^2, R^3 = H, Me

Tris(2-methyl-2-phenylpropyl)tin hydride (trineophyltin hydride, Nph_3SnH) and deuteride were synthesized by Mascaretti et al. and applied to the reduction of organic halides and α-haloketones and to the synthesis of 6-halopenicillanate analogues of β-lactamase inhibitors.[143] The reaction of trineophyltin deuteride and carbon tetrachloride was very slow (48 h at 25 °C), but α-bromoacetophenone and α-bromo-2-acetonaphthone led to the corresponding deuterated ketones in only 2 h at 70 °C with excellent yields (98% and 87%, respectively). This methodology was extended to the chemo- and diastereoselective hydrodehalogenation of 6β-halo-6α-fluoropenicillanates **124** with both trineophyltin hydride and deuteride to give the corresponding 6β-fluoropenicillanates or 6β-fluoro-α-deuteriopenicillanates **125**, respectively (Scheme 47).

Scheme 47[a]



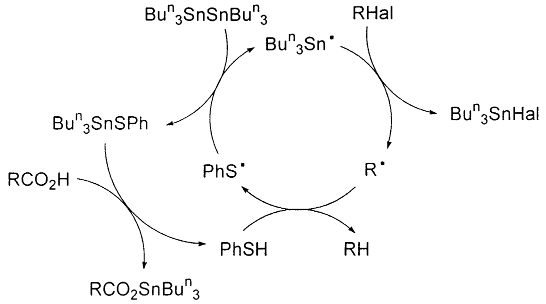
R = $PhCH_2$, Ph_2CH, $Bu^tCO_2CH_2$
X = Br, Cl

[a] Reagents and conditions: i, $Nph_3SnH(D)$, AIBN, THF, rt, 12 h.

The novel tin hydride dibutyl-4,7,10-trioxaundecylstannane, $CH_3(OCH_2CH_2)_2O(CH_2)_3SnBu^n{}_2H$, containing a polar tail, was synthesized in an attempt to accomplish the easy separation of organic reaction products from organotin species by silica gel chromatography.[144] The reduction of hexadecyl halides in benzene at reflux and in the presence of AIBN gave the following information.[145] The corresponding bromide and iodide were completely reduced to hexadecane with a slight excess of hydride in only 1 and 2 h, respectively. On the other hand, the chloride required an excess of hydride and longer reaction time (18 h). Standard chromatography techniques allowed the isolation of hexadecane in 85−95% yield and the recovery of the tin halide in 95% yield, which in addition was transformed into the above hydride by reaction with LAH (50−60%).

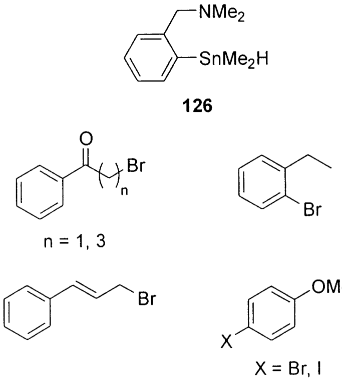
Hexabutylditin (HBDT, $Bu^n{}_3SnSnBu^n{}_3$) together with malonic acid and benzenethiol as catalyst was an effective replacement for TBTH in the radical-chain reduction of organic halides.[146] In this system the actual hydrogen donor is the thiol, the radical of which displaces tributylstannyl radicals from HBDT, the carboxylic acid reacting with $Bu^n{}_3SnSPh$ to regenerate the thiol according to Scheme 48. The reactions were performed with 5 mol % benzenethiol and 5 mol % AIBN in refluxing benzene, the reduction proceeding successfully for the following substrates: 1-iodododecane (95%), 2-bromoadamantane (97%), 1-bromoadamantane (95%), α-bromoacetophenone (99%), ethyl 2-bromohexanoate (86%), *p*-bromobenzyl bromide (95%), and methyl 2-iodobenzoate (85%). In the case of neophyl bromide, rearrangement of the corresponding radical to give mixtures of *tert*-butylbenzene and isobutylbenzene was observed with *tert*-butylperoxycyclohexane in refluxing toluene, the product ratio depending on the amount of benzenethiol in the reaction medium.

Scheme 48



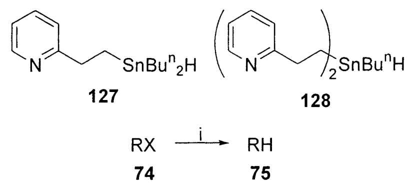
Vedejs et al. found that the hydride **126**, [*o*-(dimethylaminomethyl)phenyl]tin hydride, was internally activated for both nucleophilic hydride transfer and radical-chain reduction, depending on the solvent. The nucleophilic hydride pathway was favored in methanol and used for the selective reduction of ketones. On the other hand, when THF was used as solvent, the radical-chain dehalogenation of various alkyl and aryl bromides and iodides was achieved at room temperature and in the absence of radical initiators (Chart 12).[147] Simple alkyl bromides were efficiently dehalogenated on a time scale of hours, whereas longer reaction times were needed for aryl halides. Deliberate addition of galvinoxyl suppressed the reductive dehalogenation as expected for a chain process.

Chart 12. Dehalogenation of Organic Halides with 126 in THF at 20 °C for 1 h to 3 d



The potential of intramolecular coordination for the control of radical reactions was demonstrated for hydrides having pyridyl groups, **127** and **128**.[148] The reduction of organic halides **74** exhibited unique features in contrast to those with TBTH. Primary alkyl bromides were reduced smoothly with **127**, but the corresponding chlorides, as well as *sec*-alkyl and aromatic chlorides, remained unchanged under the same conditions (Scheme 49). However, all chlorides were reduced by TBTH, albeit slowly. With compound **128**, organic iodides were reduced smoothly, the reactions with organic bromides being much slower and the organic chlorides showing no activity. Thus, the introduction of the second pyridyl group further decreased the reactivity of the tin radical, but made easier the separation and recovery of the tin halide

Scheme 49[a]



127 **128**

74 **75**

	TBTH	**127**	**128**
X = Cl	12-75%	0%	0%
X = Br	93-100%	90-99%	20-56%
X = I	96-100%	97-99%	94-97%

R = n-$C_{12}H_{25}$, $Ph(CH_2)_3$, 1-naphthyl, n-$C_8H_{17}CHCH_3$

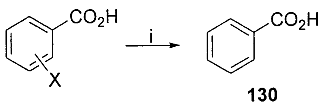
[a] Reagents and conditions: i, TBTH, **127** or **128**, AIBN, PhH, 60 °C, 2 h.

after the reaction. It was remarkable that the reduction of alkyl halides could be modulated or even completely suppressed in the presence of bipyridyl, clearly indicating the effect of intermolecular coordination on the reactivity of the tin radical.

The solubility of TBTH has practically limited its use to organic solvents. To perform tin radical chemistry in water, Breslow et al. designed and synthesized a tin hydride, $[MeO(CH_2)_2O(CH_2)_3]_3SnH$, able to reduce alkyl bromides and iodides in water with chemical or sunlamp initiation.[149] For instance, mono-6-iodo-β-cyclodextrin was reduced in water to 6-deoxy-β-cyclodextrin in 76% yield, with 4,4′-azobis-(4-cyanovaleric acid) (ACVA) at 80−90 °C for 2 h. *m*-Bromobenzoic acid, 6-bromo-6-deoxy-α-methylglucopyranoside, and 2-bromopentanoic acid were debrominated in 5% sodium hydrogen carbonate or water at room temperature using a sunlamp for 40 min in 88%, 84%, and 37% yield, respectively. In benzene solution, 1-bromooctane was reduced to octane with AIBN in 99% yield. One main advantage of this methodology is the possibility to regenerate the tin hydride by treatment with hydrochloric acid, followed by reduction of the trialkyltin chloride with borane.

Maitra et al. utilized detergents such as cetyltrimethylammonium bromide, cetyltrimethylammonium chloride, sodium dodecyl sulfate, or Triton-X-100 to solubilize TBTH in water and therefore achieve the dehalogenation of water-soluble halides in aqueous media. These conditions allowed the efficient dehalogenation of sodium 3-bromobenzoate, the presence of the detergent also being necessary for the complete dehalogenation of water-insoluble substrates such as 9-bromoanthracene (85% yield of anthracene). Deeper research pointed out that no other additive but sodium hydrogen carbonate was enough to accomplish the dehalogenation of water-soluble organic halides in water by TBTH, preformed TBTH, and triphenyltin hydride (TPTH).[150] Under these conditions, *o*-, *m*-, and *p*-bromo- and -iodobenzoic acids **129** were reduced in high yields at 90 °C for 24 h (Scheme 50). TPTH was also found to effect the dehalogenation in high yields at 90 °C but in only 6 h. Other substrates subjected to dehalogenation were 5-bromouracil (>95% yield with no additive) and cholesterol dibromide (92% yield).

Scheme 50[a]



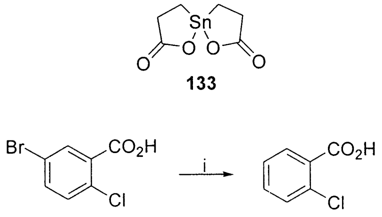
129 **130**

X = Br, I (80-90%)

[a] Reagents and conditions: i, TBTH or TPTH, H_2O, $NaHCO_3$, 90 °C, 24 or 6 h.

In another report, Collum et al. described the reduction and free radical cyclizations of alkyl and aryl bromides carried out in aqueous base by sodium borohydride in the presence of the base-soluble dialkyltin(IV) reagent **133** and 4,4′-azobis(4-cyanovaleric acid).[151] This system was applied to the debromination of *m*-bromobenzoic acid and 2-chloro-5-bromobenzoic acid (**131**) in aqueous potassium hydroxide at 80 °C for several hours, giving rise to benzoic acid and 2-chlorobenzoic acid (**132**), respectively, in >90% yield (Scheme 51). It should be noted that a resistance of alkyl and aryl chlorides was observed. Although the role of tin(IV) species and the mechanism were not clarified, it seemed that sodium borohydride was the hydrogen source, as demonstrated by experiments carried out with $NaBH_4$−D_2O and $NaBD_4$−D_2O.

Scheme 51[a]



133

131 **132**

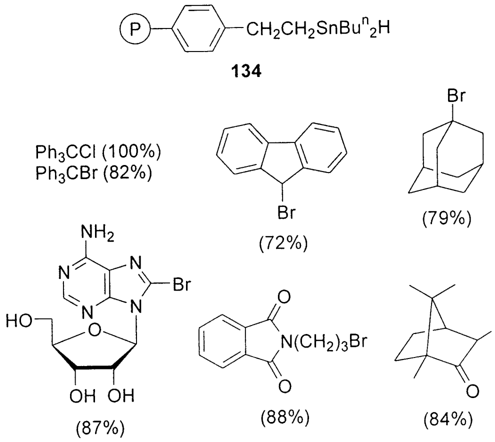
(>90%)

[a] Reagents and conditions: i, **133**, $NaBH_4$, ACVA, aq KOH, 80 °C.

As mentioned before, one major drawback of TBTH is the separation of their derived products from the desired reaction products. Attempts to overcome this inconvenience were carried out by Neumann et al., who in the early 1990s developed a polymer-supported organotin hydride, **134**.[152] The new organotin reagent was based on cross-linked polystyrene of large pore size,[116] where the tin moiety was separated from the aromatic nucleus by two methylene units. The reagent proved to be insoluble in common organic solvents and could be easily separated and regenerated. It found practical application in the dehalogenation of bulky halides such as 9-bromofluorene, trityl bromide and chloride, or 1-bromoadamantane.[152b] Chemoselective reductions were also observed, not interfering with some oxygen- and nitrogen-containing functional groups (Chart 13). In all experiments, the polymer had reactivity and selectivity similar to those of TBTH.

The above-mentioned methodology was extended by Dumartin et al., who synthesized polystyrene-supported organotin hydrides, polymer−$(CH_2)_n$-$SnBu^n_2H$ with equal ($n = 2$) or longer ($n = 3, 4$) spacer chains, by reaction of ω-haloalkylpolystyrenes with

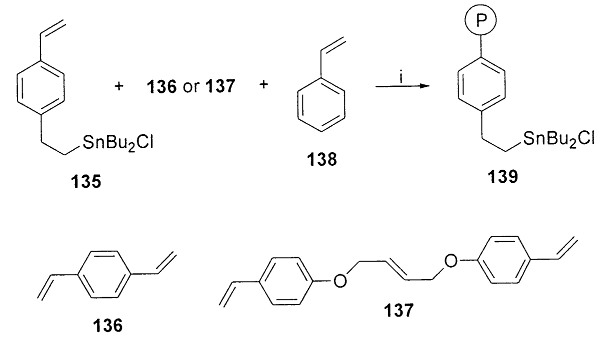
Chart 13. Dehalogenation of Organic Halides with 134 and AIBN in PhH or PhMe at 60 °C for 4 h



hydridodibutylstannyllithium.[153a–d] The reduction efficiency of these polymer hydrides was monitored by reduction of 1-bromodecane and 3-iodo-5-cholestene, leading to yields similar to those obtained with TBTH. Easy separation and regeneration of the hydride together with the low levels of organotin pollution detected were the main advantages. Further work was developed to implement the in situ and catalytic generation of polymer-supported organotin hydrides from the corresponding halides.[153e] In this study, the polymer–$(CH_2)_4SnBu^n{}_2I/NaBH_4$ system proved to be more efficient than the polymer–$(CH_2)_2SnBu^n{}_2Cl/NaBH_4$ system in the reduction of 1-bromoadamantane (93% yield of adamantane with 20 mol % vs 40% yield with 50 mol %, respectively). The former organotin halide polymer was recovered and reused without significant loss of activity, showing very low residual tin pollution levels (blank to 34 ppm) in comparison with the latter (530–1975 ppm) or with $Bu^n{}_3SnCl$–$NaBH_4$ (10^5 ppm).

Macroporous beads **139** bearing organotin moieties were synthesized by suspension copolymerization of a convenient tin monomer, **135**, with styrene (**138**) and a cross-linking agent, **136** or **137**, in the presence of a porogen (Scheme 52).[154] These macroporous materials are characterized by a permanent porous structure which does not collapse in the dry state. The use of divinylbenzene (DVB) (**136**) or (*E*)-1,4-bis(4-vinylphenoxy)but-2-ene (**137**) as cross-linker, and decane or 2-ethylhexanol as porogen, led to a series of macroporous resins **139** with adjustable tin-loading and cross-linking levels. The dehalogenation of 1-bromoadamantane was chosen as a test reaction to study the catalytic efficiency of these supports. In general, all of them showed good reactivity for the reaction performed when the amount of **139** was maintained at 10 mol % with respect to 1-bromoadamantane, sodium borohydride being in a 2-fold excess. The supports cross-linked with **137** were more efficient (75% conversion in 30 min) than those cross-linked with **136**, low activity being observed for nonporous supports (15% conversion in 30 min). The intrinsic stability of the reactive supported tin species was very high as confirmed by several successive reuses without loss of activity and without need of regeneration.

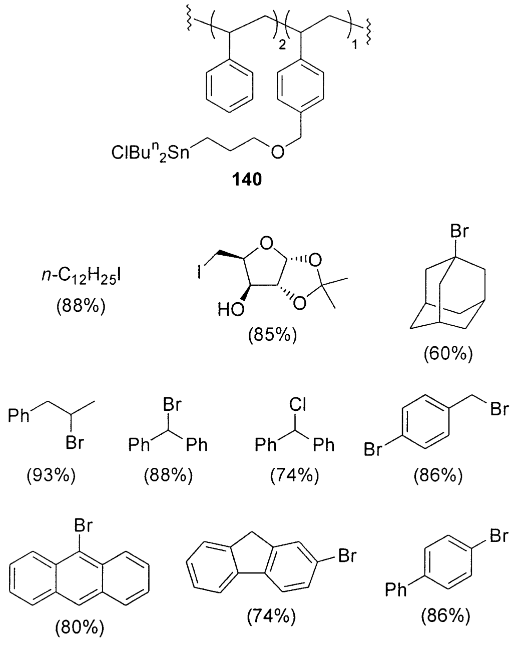
Scheme 52[a]



[a] Reagents and conditions: i, decane or 2-ethylhexanol, AIBN, 80 °C, 8 h.

Organotin reagent on non-cross-linked polystyrene, **140**, is soluble in most organic solvents and highly efficient in the catalytic free radical reduction of a variety of organic halides.[155] Because a single phase was utilized with non-cross-linked polystyrene, the reactions rates were up to 100 times faster than those of standard cross-linked solid-phase methods. This reagent was prepared by copolymerization of styrene and *p*-chloromethylstyrene, followed by S_N2 displacement with allylic alcohol and final photochemical hydrostannylation using chlorodi-*n*-butylstannane. Primary, secondary, tertiary, and aromatic bromides, as well as primary iodides and a secondary chloride, were hydrodehalogenated with a catalytic amount of **140** and sodium borohydride in dimethylacetamide (DMA), in moderate to excellent yields (Chart 14). The method was also found convenient for the regioselective benzylic dehalogenation of *p*-bromobenzyl bromide, and in addition led to minute levels (540 ppm) of residual tin pollution.

Chart 14. Catalytic Dehalogenation of Organic Halides with 140 (0.01–0.20 equiv) and $NaBH_4$ (1.5 equiv) in DMA at 80 °C for 0.5–24 h



V. Group VA and VIA Metals

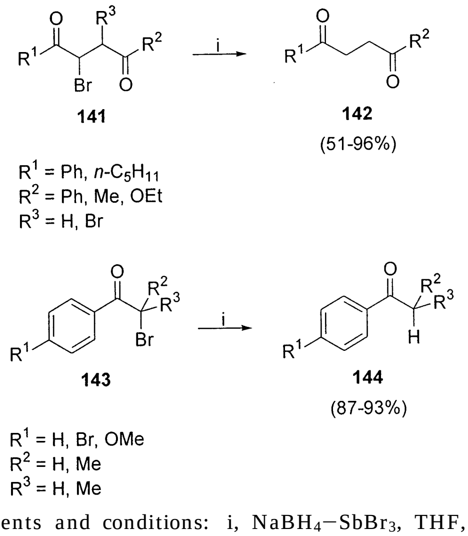
As the title of the review indicates, only metal-involved hydrodehalogenation reactions are being described, and therefore phosphorus or sulfur reagents will not be covered in this review. Nonetheless, we believe it could be of interest to the reader to provide some references related to these topics. The following reductive dehalogenations of organic halides were accomplished with phosphorus compounds: phenylhaloacetylenes,[156] α-bromocarboxylates,[157a] benzylic halides,[157b] and 1,1-dibromoalkenes[158] with dialkyl phosphites; 2-halothiazoles[159] and triphenylmethyl halides[160] with tertiary phosphines; α-halocarbonyl compounds with phosphorous acid,[161] triphenylphosphonium iodide,[162] and polymer-supported triphenylphosphine;[163] a series of organic halides (radical-chain dehalogenation) with dialkyl phosphites[164a,b] and hypophosphorous acid.[164c,d,165]

Concerning the use of sulfur reagents, perfluoroaryl halides were dehalogenated by sodium hydroxymethanesulfinate, sodium dithionite, and aminoiminomethanesulfinic acid.[166] Hydrogen sulfide and thiol-containing regents were used in the reductive dehalogenation of 21-iodo derivatives of corticosteroids,[167] and of hexachloroethane, carbon tetrachloride, and bromoform.[168] Finally, sodium dithionite also found application in the reductive dehalogenation of α-haloketones[169] and carbon tetrachloride.[170]

A. Antimony

The sodium borohydride–antimony tribromide combination was found to be chemoselective for the reductive debromination of 2-bromo- and 2,3-dibromo-1,4-butanediones **141** and aromatic α-bromoketones **143** to give the corresponding diketones **142** and aromatic ketones **144**, respectively (Scheme 53).[171] The optimum conditions for the reduction required an equal molar equivalent of antimony tribromide, relative to sodium borohydride, to suppress the 1,2-reduction of ketones and three molar equivalents of antimony tribromide and sodium borohydride, relative to the substrate, to give the products in high yields. On the other hand, α-chloroketones as well as aliphatic α-bromoketones and α-bromoesters were recovered unchanged.

Scheme 53[a]



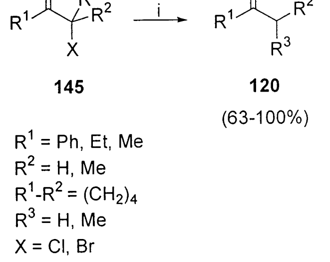
[a] Reagents and conditions: i, $NaBH_4$–$SbBr_3$, THF, DMSO, 0–22 °C, 3.5–20 h.

Diphenylantimony hydride (Ph_2SbH) in the presence of AIBN emerged as an alternative to TBTH in the radical dehalogenation of organic halides.[172] Thus, 1-bromoadamantane, dibromocholestanol, 2-chloroacetophenone, and cinnamic acid chloride were dehalogenated by diphenylantimony hydride in 10 mol % AIBN in yields ranging from 53% to 98%. Under these reaction conditions, benzoyl chloride was transformed into benzyl benzoate, whereas 1,1,1-trichloromethylbenzene was reduced to 1,1-dichloromethylbenzene with 10 mol % palladium dichloride instead of AIBN.

B. Selenium and Tellurium

Bis(triphenylstannyl) telluride [$(Ph_3Sn)_2Te$], in combination with potassium fluoride dihydrate, allowed the efficient reductive dehalogenation of α-chloro- and α-bromoketones **145** in high yield and under very mild reaction conditions (Scheme 54).[173a] The process was suggested to take place through the tellurium intermediate species Ph_3SnTeH or $R^1COCR^2R^3TeH$. In some cases, better yields were observed when the reaction was carried out under reflux, whereas very low yields were obtained in the absence of potassium fluoride dihydrate or when cesium fluoride was used instead. Further work on this topic led to the investigation of similar reagents such as bis(triphenylstannyl) selenide [$(Ph_3Sn)_2Se$] and bis(*tert*-butyldimethylsilyl) telluride [$(TBDMS)_2Te$]. Both reagents allowed the effective reductive dehalogenation (48–94% yield) of α-halo aromatic ketones in the presence of potassium fluoride dihydrate and acetonitrile at room temperature for 24 h.[173b] However, bis(triphenylstannyl) selenide was considered the reagent of choice since it has no significant odor, it is not water sensitive, and it can be stored in the refrigerator over long periods of time without any trace of decomposition. A mechanism involving the intermediacy of enolate species was suggested and confirmed by trapping it with benzaldehyde.

Scheme 54[a]

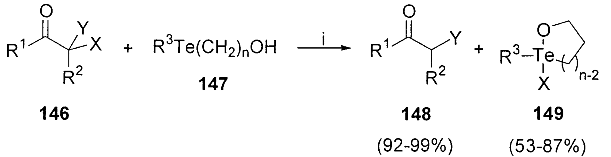


[a] Reagents and conditions: i, $(Ph_3Sn)_2Te$, $KF{\cdot}2H_2O$ (3 equiv), CH_3CN (or CD_3CN), rt, 0.2–10 h.

Sodium hydrogen telluride (NaTeH), generated in situ from tellurium powder and sodium borohydride, was reported to dechlorinate triphenylmethyl chloride in DMF at 70 °C to give triphenylmethane in 87% yield.[174] 9-Bromofluorene led to a mixture of fluorene and bisfluorene, whereas benzylic halides of the type $ArCH_2Cl$ furnished the corresponding aromatic aldehydes by decomposition of the tellurium species $ArCH_2TeH$. The above reagent seems to have only practical application in the dehalogenation of the tertiary chloride.

Tellurides **147**, containing a hydroxy group on the side chain, were readily converted into cyclic halo-oxatelluranes **149** by dehalogenation of α-halocarbonyl compounds **146** (Scheme 55).[175] The reactivity observed followed the order iodide > bromide > chloride, but the elongation of the hydroxypolymethylene chain from three to four carbons had little effect on the reactivity. Higher halophilicity was observed for tellurides in comparison with selenides, no product or low yields being detected for the reactions examined with the latter.

Scheme 55[a]



R^1 = Ph, p-BrC_6H_4, OEt
R^2 = H, CO_2Et
R^3 = Me, Et, Ph, $HO(CH_2)_3$, $HO(CH_2)_4$
X = Cl, Br, I
Y = H, Br
n = 2, 3

[a] Reagents and conditions: i, CH_2Cl_2, rt (or reflux), 1.5−8 h.

VI. Transition Metals

Transition metals have become important reagents in organic synthesis since the begining of the last century and have been used in the hydrodehalogenation of organic halides[176] under different forms, including zerovalent metals, bimetallic systems, metal salts, organometallic compounds and complexes, or supported metals, among others. Besides the nature of the metal-containing agent, other parameters have to be taken into account such as the homogeneous or heterogeneous conditions of the reaction, hydrogen source, particle size effect, surface area, or metal−support interaction.[177] Thus, many possible combinations are available to carry out the above-mentioned transformation, the system of choice depending on many factors such as the type of substrate, catalytic activity, scale and economy of the process, possibility to reuse the catalyst, or environmental impact. Among the different metals we will deal with in this section, an important part of it will be dedicated to palladium, which by far is the most used metal in hydrodehalogenation reactions.

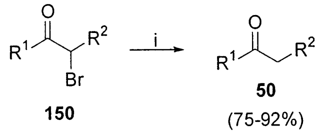
A. Group IVB: Ti, Zr

Titanium and zirconium complexes have become highly interdisciplinary compounds embracing inorganic, organic, organometallic, and polymeric research areas.[178] Those containing cyclopentadienyl ligands have been of special interest in organic chemistry as reducing agents or as catalysts in hydrodehalogenation reactions, in the latter case normally combined with Grignard reagents or metal hydrides.

1. Titanium

Dicyclopentadienyltitanium chloride and bromide (Cp_2TiX, X = Cl, Br), prepared in situ from the reduction of dicyclopentadienyltitanium dichloride with isopropylmagnesium chloride and bromide, respectively, were effective dehalogenating reagents for α-bromoketones **150** (Scheme 56).[179] A 2 equiv sample of reagent is required to complete the reaction: the first equivalent possibly abstracts the bromine atom of the α-bromoketone, and the resulting radical combines with the second equivalent to form a stable titanium enolate, the hydrolysis of which gives the reduction product **50**.

Scheme 56[a]

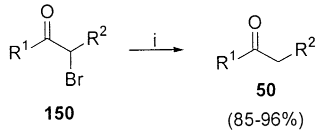


R^1 = Me, Ph, p-BrC_6H_4
R^2 = H, Me

[a] Reagents and conditions: i, Cp_2TiCl, THF, rt, 5 h.

α-Bromoketones were also reduced by the dicyclopentadienyltitanium dichloride−samarium combination. It was found that dicyclopentadienyltitanium dichloride was reduced by samarium powder. In this reaction a samarium multinuclear complex of the type $[Cp_2TiCl]_2SmCl_2$ was believed to be formed including divalent samarium and low-valent titanium species. With this system, a series of α-bromoketones **150** were transformed into the corresponding debrominated ketones **50** in good yields under mild and neutral conditions (Scheme 57).[180]

Scheme 57[a]



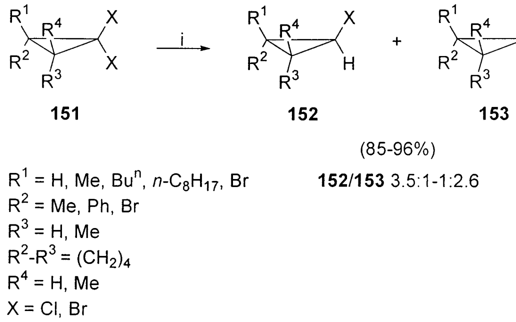
R^1 = Ph, p-BrC_6H_4
R^2 = H, Me

[a] Reagents and conditions: i, Cp_2TiCl_2, Sm, THF, rt, 1 h.

In the early 1990s the partial reductive dehalogenation of substituted *gem*-dichlorocyclopropanes with LAH or DIBAL (diisobutylaluminum hydride) containing $Ti(OBu^n)_4$, $TiCl_4$, or Cp_2TiCl_2 in refluxing dioxane or ether was reported. Mixtures of *cis*- and *trans*-monochlorocyclopropanes were obtained in 3:1 to 5:1 ratio with very high conversion (98%). The reaction extended to substituted *gem*-dibromocyclopropanes led mainly to the fully reduced hydrocarbons.[181]

It is also known that Grignard reagents can achieve the hydrodehalogenation of different substrates when promoted by titanium compounds. For instance, Baird et al. reported that 1,1-dihalocyclopropanes could be converted into the corresponding monohalocyclopropanes by reaction with ethylmagnesium bromide and a small amount of titanium tetraisopropoxide.[182a] The methodology was applied to both 1,1-dibromo- and 1,1-dichlorocyclopropanes **151**, where appropriate giving rise to the mixture of diastereoisomers **152** and **153** (Scheme 58). In the presence of an excess of ethylmagnesium bromide, the nonhalogenated cyclopropane was the product

Scheme 58[a]

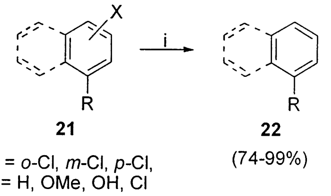


[a] Reagents and conditions: i, EtMgBr, Ti(OPr^i)$_4$ (2−10 mol %), Et$_2$O, 20 °C, 10−30 min.

obtained from the corresponding dibromide in >90% yield. Other Grignard reagents were also effective, labeling studies indicating that the hydrogen introduced into the cyclopropane ring was not derived from either the α- or *β*-position of the Grignard reagent.[182b] Thus, the reduction with phenethylmagnesium bromide in *d*$_8$-tetrahydrofuran led to both diastereomeric deuterated monobromides.

Takahashi et al. described the catalytic dechlorination of aromatic chlorides using Grignard reagents in the presence of catalytic amounts of dicyclopentadienyl titanium dichloride.[183] The best results were obtained with *n*-butylmagnesium bromide, THF as solvent dramatically improving the yield of the reaction. Various chloroanisoles, chloronaphthalenes, and chlorophenols **21** were effectively dechlorinated, monodechlorination of 2,4-dichloroanisole also being achieved in 66% yield (Scheme 59). Titanium species of the type Cp$_2$Ti^{III}H, hydridomagnesium species, and direct *β*-hydride transfer from an alkyl substituent on titanium metal were suggested as plausible intermediates.

Scheme 59[a]

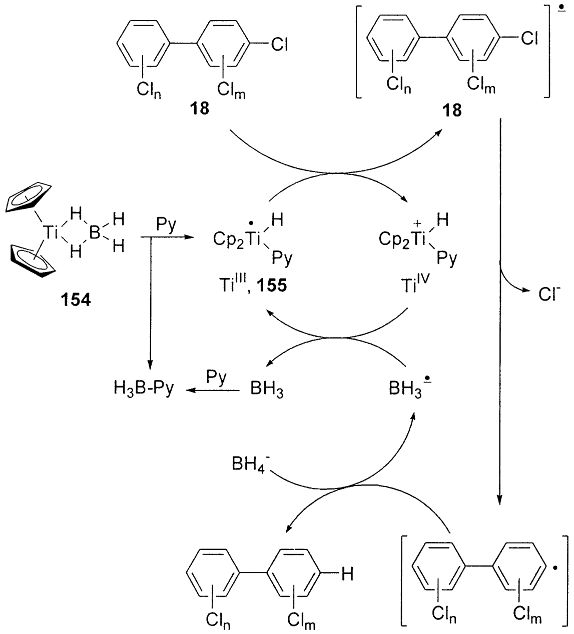


[a] Reagents and conditions: i, Bu^{n}MgCl, Cp$_2$TiCl$_2$ (10 mol %), THF, −78 °C, 0.5−48 h.

The titanium complex catalyzed reduction of aromatic halides by sodium borohydride in different solvents has been studied in detail by Schwartz et al. In a preliminary report, it was observed that when the reaction was conducted in DMF, a borohydride−DMF adduct was formed, tentatively formulated as NaBH$_3$(OCH$_2$NMe$_2$), and considered the actual reducing agent.[184a] This new species was able to reduce and dimethylaminate organic halides by a nonradical, likely nucleophilic pathway. Further work revealed that a change of solvent from DMF to dimethylacetamide (DMA) allowed the smooth reduction of aryl halides with no significant solvent intervention, therefore entirely changing both the actual reducing agent and reaction mechanism.[184b] Taken together, relative rate measurements (carried out for *para*-substituted bromobenzenes), radical "clock" cyclization probes, and deuterium-labeling studies pointed to a mechanism for aryl halide reduction by the Cp$_2$TiCl$_2$−NaBH$_4$−DMA system based on electron transfer from a titanium complex catalyst and radical formation and trapping. Titanocene borohydride, Cp$_2$Ti(BH$_4$), was considered the active species for reduction of aryl halides in ethereal solvents such as diglyme.[184c] In this case, reaction promotion was observed by the addition of amines, which cleave titanocene borohydride to give borane−amine and titanium−amine adducts. A synergistic effect was observed for a mixture of aliphatic and aromatic amines, the most plausible active species for aryl halide reduction being a (Cp$_2$TiH)−amine adduct.

This methodology was successfully applied to the conversion of PCBs **18** (Arochlor 1248) to readily biodegradable biphenyl, both in simple solution and, importantly, on contaminated soils.[184d] It was noted that the reduction rates were dependent on the structure of the added amine, simple aliphatic amines being less effective catalysis promoters than unhindered pyridines, with the same synergistic effect described above. Cleavage of the borohydride ligand of Cp$_2$Ti(BH$_4$) (**154**) apparently occurred to give a coordinatively unsaturated moiety (Cp$_2$TiH), which by coordination of pyridine would lead to the coordinatively saturated active catalyst **155** (Scheme 60).

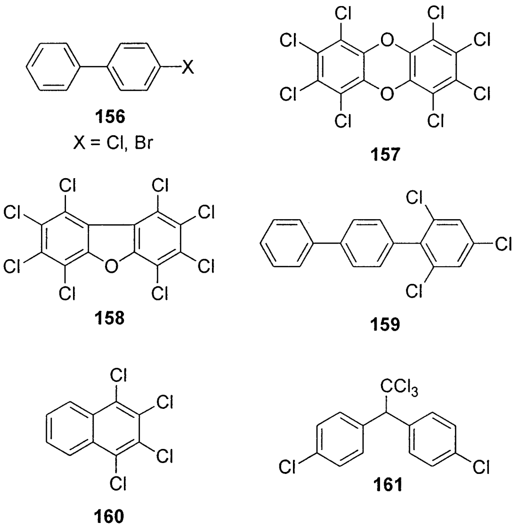
Scheme 60. Proposed Electron-Transfer Mechanism for PCB Reduction with the Cp$_2$TiCl$_2$−NaBH$_4$−Amine System



The titanium−borohydride−amine system was extended to the effective dehalogenation of a broad variety of aryl halide environmental pollutants such as 4-halobiphenyls **156**, octachlorodibenzo-*p*-dioxin (**157**), octachlorodibenzofuran (**158**), 2,4,6-trichloro-*p*-terphenyl (**159**), 1,2,3,4-tetrachloronaphthalene (**160**), and DDT (**161**), under mild reaction conditions (Chart 15).[184e]

The above methodology involving titanocene chloride, in conjunction with sodium borohydride and

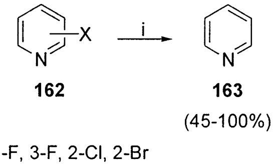
Chart 15. Complete Dehalogenation of Aromatic Halides with Cp_2TiCl_2, $NaBH_4$, Diglyme, and Pyridine at 125 °C for 4−18 h



pyridine, was extended by other authors to the dechlorination of PCB Arochlor 1242, yielding biphenyl.[185] The dechlorination process resulted in a transient increase in concentration of the monochlorinated biphenyls, particularly 3-chlorobiphenyl. Dechlorination in the presence of alternative amines or in PCB-contaminated soils proceeded at reduced rates and yielded mono- and dichlorobiphenyls in the final product mixture.

Woo et al. reported the dehalogenation of monohalopyridines **162** catalyzed by group IVB metallocene reagents of the type $Cp^{\blacklozenge}{}_2MX_2$ ($Cp^{\blacklozenge}$ = Cp or Cp^*; Cp = η^5-C_5H_5; Cp^* = η^5-C_5Me_5; M = Ti, Zr, Hf), in the presence of different hydrides at room temperature to give pyridine (**163**).[186] The catalytic activity was observed to decrease in the order Ti > Zr > Hf; M−F ≈ M−Cl ≈ M-Br ≈ M−I; Cp_2M > $CpCp^*M$ > $Cp^*{}_2M$; Red-Al > N-selectride > K-selectride > L-selectride ≫ DIBAL; 2-fluoropyridine > 3-fluoropyridine; C−F > C−Cl > C−Br. The rate of the reaction was boosted by adding 4 Å molecular sieves, although all catalyst combinations were ineffective in the defluorination of fluorobenzenes and perfluorodecalin (Scheme 61).

Scheme 61[a]

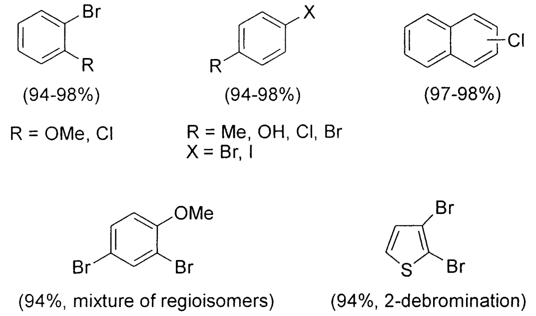


[a] Reagents and conditions: i, Cp_2TiCl_2, Red-Al, 25 °C, 36 h.

2. Zirconium

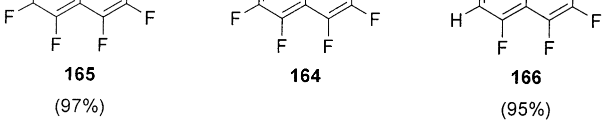
Takahashi et al. described zirconocene derivative induced dehalogenation of aromatic halides. In a preliminary study, this group discovered that stoichiometric amounts of $Cp_2ZrBu^n{}_2$ (Negishi reagent) were able to dehalogenate various aromatic halides at room temperature and in very high yields (90−98%).[187a,b] The catalytic version of this reaction was accomplished with zirconocene dichloride and an excess of an alkylmagnesium reagent, *n*-butylmagnesium chloride being the most satisfactory one (Chart 16).[187c] Methylmagnesium bromide was ineffective, thus indicating that the reduction requires a *β*-hydrogen on the alkylmagnesium reagent to transfer the hydrogen to the aromatic ring. Several dihalobenzenes were also tested, the halogen reactivity found following the order I > Br > Cl, and therefore allowing the selective dehalogenation under adjusted reaction conditions. In all cases, overreduction of the less reactive halogen atom was negligible. Selective reduction of 2,3-dibromothiophene was achieved with high selectivity to give 3-bromothiophene in 94% yield. However, 2,4-dibromoanisole led to a mixture of regioisomeric bromoanisoles. From a mechanistic point of view, two different pathways involving oxidative addition reaction of aromatic halides to Cp_2Zr^{II} species and metal−halogen exchange were suggested.

Chart 16. Catalytic Dehalogenation of Aromatic Halides with Cp_2ZrCl_2 (10 mol %) and Bu^nMgCl (3 equiv) in THF at −78 °C to rt for 1−12 h



We have already mentioned that activation and functionalization of carbon−fluorine bonds are topics of great interest for organic chemists.[23] Richmond et al. reported the first examples of selective room-temperature hydrogenolysis of strong aromatic carbon−fluorine bonds by the soluble group IVB metallocene zirconocene dichloride, mercury(II) dichloride, and magnesium metal.[188] For instance, octafluoronaphthalene (**164**) was transformed into 1,3,4,5,6,7,8-heptafluoronaphthalene (**165**) under these reaction conditions in 2 h. Prolonged reaction times (13 h) resulted in double fluorine−hydrogen exchange to generate 1,3,4,5,7,8-hexafluoronaphthalene (**166**), the hydrogenolysis being highly regioselective (Scheme 62). Deuterium incorporation from deuterated THF indicated that the solvent was the proton source, no reactivity being exhibited with activated magnesium in the absence of the metallocene. This methodology

Scheme 62[a]



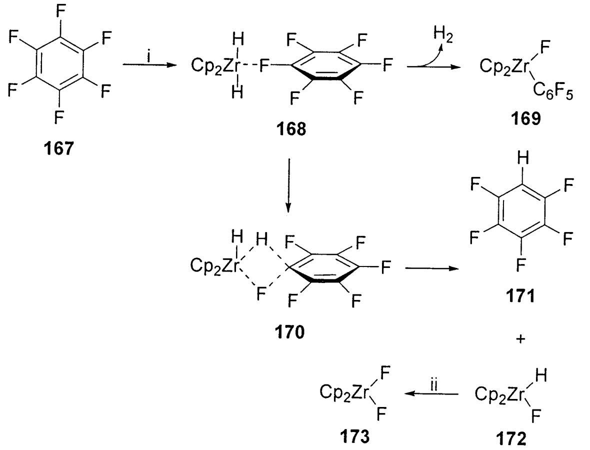
[a] Reagents and conditions: i, Cp_2ZrCl_2, Mg, $HgCl_2$ (or Me_3P), THF, rt, 2 h; ii, Cp_2ZrCl_2, Mg, $HgCl_2$ (or Me_3P), THF, rt, 13 h.

was extended to the reduction of hexafluorobenzene to furnish quantitatively pentafluorobenzene or 1,2,4,5-tetrafluorobenzene in 2 and 24 h, respectively. Alternatively, trimethylphosphine could be used instead of mercury(II) chloride. A mechanistic rationale consistent with the results obtained was proposed involving the formal oxidative addition of the aromatic carbon−fluorine bond at a low-valent "Cp_2Zr", followed by the rapid homolytic cleavage of the zirconium−carbon bond and abstraction of hydrogen from the THF by the resulting pentafluorophenyl radical.

Vinylic carbon−fluorine activation in 1,1-difluoroolefins was also accomplished with a low-valent zirconocene to generate stereoselectively 1-fluorovinylzirconocene, the protonolysis of which yielded the corresponding monodefluorinated *cis*-olefins.[189]

The zirconium hydride $(Cp_2ZrH_2)_2$ reacted with hexafluorobenzene (**167**) to give the carbon−fluorine activation product $Cp_2Zr(C_6H_5)F$ (**169**). Mechanistic studies were consistent with an initial association between the zirconium metal center and C_6F_6 via fluorine, **168**. Such an interaction may lead to ligand-assisted loss of molecular hydrogen or cyclopentadiene and carbon−fluorine activation, resulting in the formation of a zirconium−fluorine bond. Competitively, a σ-bond metathesis between the zirconium hydride and C_6F_6 may also occur, giving rise to a new zirconium fluoride complex, **173**, and pentafluorobenzene (**171**) (Scheme 63). A similar mechanism was postulated for the hydride Cp_3ZrH.[190a] Activation of aliphatic and aromatic carbon−fluorine bonds was also achieved with $Cp^*_2ZrH_2$.[190b,c] Primary, secondary, and tertiary monofluorinated aliphatic hydrocarbons (1-fluorohexane, fluorocyclohexane, and 1-fluoroadamantane, respectively) reacted with $Cp^*_2ZrH_2$ at ambient temperature under an atmosphere of hydrogen, giving the corresponding alkanes quantitatively through a radical mechanism. On the other hand, reaction of $Cp^*_2ZrH_2$ with monofluoroarenes involved hydridic attack on the aromatic ring and subsequent fluoride abstraction to yield Cp^*_2ZrHF and the hydrogenated arene, through a mechanism similar to that depicted in Scheme 63.

Scheme 63[a]



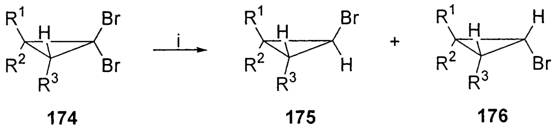
[a] Reagents and conditions: i, $(Cp_2ZrH_2)_2$, THF, 65 °C; ii, **171**.

The partial reductive dehalogenation of substituted *gem*-dichlorocyclopropanes and total dehalogenation of *gem*-dibromocyclopropanes previously reported with LAH or DIBAL and titanium compounds was also accomplished with zirconium derivatives $ZrCl_4$, Cp_2ZrCl_2, and $Zr(acac)_4$.[181]

B. Group VB: V

Vanadium species in low oxidation states serve as versatile one-electron reductants.[191] A combination of a vanadium(II) species, generated from vanadium(III) chloride and zinc, in the presence of either diethyl phosphonate or triethyl phosphite, was reported to effect the highly stereoselective reduction of *gem*-dibromocyclopropanes **174** (Scheme 64).[192]

Scheme 64[a]



(17-99%)

R^1 = H, Ph, CN, CO_2Me

175/**176** 93:7-1:>99

R^2 = H, Me

R^3 = H

R^2-R^3 = $(CH_2)_4$

[a] Reagents and conditions: i, VCl_3, Zn; $P(OR)(OEt)_2$, R = H, Et; DME, rt (or 80 °C), 24−120 h.

Cyano or methoxycarbonyl substitution on the cyclopropane ring resulted in more facile reduction. It is worthy to note that a catalytic reduction process was also achieved when the amount of vanadium(III) chloride was decreased, the complex $CpV(CO)_4$ giving better yields and stereoselectivity than VCl_3. The reaction was proposed to take place through the corresponding radical and/or carbanion by one-electron reduction, in which the phosphorus component increases the reduction capability by coordination.

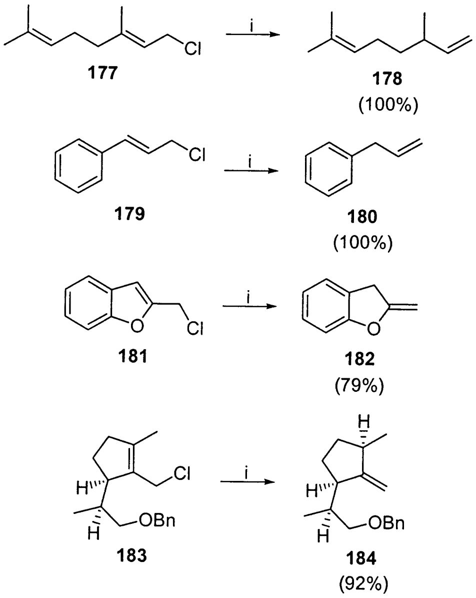
C. Group VIB: Cr, Mo, W

1. Chromium

Lithium chromium(I) dihydride ($LiCrH_2$), prepared by alkylative reduction of chromium(III) chloride with *n*-butyllithium, was found to be a versatile reducing agent applied to the reductive metathesis of carbon−halogen bonds in aryl or alkyl halides.[193] Reactions were performed in THF at 25 °C for 12 h, aryl chlorides, bromides, and iodides being dehalogenated to the corresponding arenes in yields higher than 93%.

Chromium(II) species, generated from chromium(III) chloride and LAH, have been recently applied to the double bond migrative reduction of allylic chlorides, giving rise to the less substituted olefins through a six-membered transition state in which the allylchromium intermediate suffers protonation at the γ-position.[194] The reaction proceeded with high regioselectivity under mild and neutral conditions. Some of the substrates covered in this study are geranyl chloride (**177**), cinnamyl chloride (**179**), 2-chloromethylbenzo[*b*]furan (**181**), and (3*R*,8*S*)-7-chloro-1-iridene derivative **183** (Scheme 65). Regioisomeric

Scheme 65[a]



[a] Reagents and conditions: i, $CrCl_3$, LAH, Pr^iOH, THF, DMF, rt, 15−24 h.

ratios were >95:5, except in the case of **181**, where the regioisomer of **182** was also obtained in 16% yield.

2. Molybdenum and Wolframium

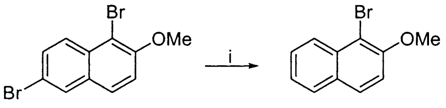
Catalytic carbon−halogen bond cleavage was studied by direct thermal reaction of halocarbon substrates with the reduced form of the poly(oxotungstate)s $H_2W_{10}O_{32}^{4-}$ and α-$PW_{12}O_{40}^{3-}$.[195] All reactions were run at 60 °C for 24 h, carbon tetrachloride, bromotrichloromethane, 1-bromodecane, cyclohexyl bromide, and *tert*-butyl bromide being the substrates covered in this review. Kinetic profiles for dehalogenation rate vs halocarbon rate structure, relative reactivities of substrates (polyhalogenated > monohalogenated; tertiary > secondary > primary halides; bromides > chlorides), and other product distribution data, in addition to the rate law, established two key points about these processes: (a) intermediate alkyl radicals were important in most if not all of these reactions; (b) carbon−halogen bond cleavage involves either electron transfer, which is probably dissociative in nature, or halogen abstraction (atom transfer) in the rate-limiting step. Finally, oxidation of alkyl radical intermediates to carbenium ions (seen when both easily oxidized tertiary radicals and some oxidized poly(oxotungstate)s are simultaneously present) or reduction to carbanions (seen in most cases) was suggested to occur. With increasing acidity more carbanion was produced, leading to higher yields of reduction products.

Several alumina-supported and unsupported molybdenum and wolframium carbide catalysts were synthesized, characterized, and studied for their activity in the dehalogenation of CFC-12 (CCl_2F_2) under a hydrogen atmosphere.[196] The unsupported carbides had lower initial conversions than supported carbides, and W_2C/γ-Al_2O_3 showed higher conversion than Mo_2C/γ-Al_2O_3. The addition of palladium to the carbide did not improve the activity, the only reaction product observed in all cases being CH_2F_2. In comparison with 1% Pd/C, higher conversions (especially with W_2C/γ-Al_2O_3) and selectivity to HFC-32 were observed with the carbide catalysts. However, the latter deactivated slowly with time (2 h), while the palladium catalyst showed little activity loss over 12 h.

Transition-metal carbides of wolframium and molybdenum were also synthesized with temperature-programmed reactions of metal oxides or passivated nitrides. Their specific chloropentafluoroethane conversion rates were at best 1 order of magnitude less than that of a reference palladium catalyst and followed the decreasing order $Mo_2C > WC > W_2C \approx WC_{1-n} > MoC_{1-n}$.[197] This group of carbides catalyzed hydrodehalogenation and dehydrofluorination, WC appearing to be as selective toward pentafluoroethane (HFC-125) as a palladium-based catalyst. The selectivity decreased in the following sequence: $W_2C > Mo_2C > WC_{1-n} > MoC_{1-n}$. All the carbide catalysts were deactivated in the early stages of the reaction, which was mainly attributed to a site-blocking phenomenon due to a strong deposit of polymeric carbon and of hydrofluorocarbon polymers.

Regioselective hydrodebromination of 1,6-dibromo-2-methoxynaphthalene (**185**) with hydrogen and a wolframium carbide catalyst, in the presence of a phase-transfer cocatalyst such as ammonium bromide, furnished 2-bromo-6-methoxynaphthalene (**186**), a pharmaceutical intermediate, in high yield and selectivity (Scheme 66).[198]

Scheme 66[a]



185 **186**

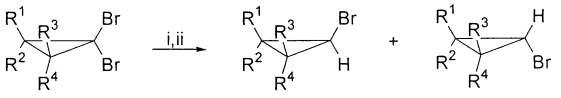
[a] Reagents and conditions: i, H_2, wolframium carbide, NH_4Br.

D. Group VIIB: Mn, Re

1. Manganese

Treatment of *gem*-dibromocyclopropanes **187** with trialkylmanganates, derived from manganese(II) chloride and 3 equiv of a Grignard reagent or alkyllithium, followed by addition of electrophiles, provided dialkylated cyclopropanes in good yields. When water was utilized as electrophile, the corresponding monoalkylated debrominated products **188** and **189** were obtained in moderate to good diastereoselectivities and yields (Scheme 67).[199] In contrast to the reaction with cuprates or zincates, which have to be performed at −48 or −85 °C, the reaction with manganates could be performed conveniently at 0 °C, THF being the solvent of choice. A reaction mechanism similar to the reaction with cuprates and zincates, in which there is an initial halogen−manganese exchange at the less hindered bromine atom, followed by alkyl migration under bromide elimination (with inversion on the cyclopropane carbon), and final protonation with retention of configuration, was assumed. The stereoselective formation of **188** was attributed to the bulkiness of the manganese reagents, which attack the less hindered halogen. The reaction was also observed to take place

Scheme 67[a]



187 **188** **189**

(56-89%)

188/189 58:42-97:3

R^1 = Me, Ph, n-C_6H_{13}, $PhCH_2OCH_2$
R^2 = H, Me
R^3 = H, Me
R^2-R^3 = $(CH_2)_4$, $(CH_2)_6$
R^4 = H, Me
R^5 = Me, Bu^n, n-C_6H_{13}, $PhMe_2Si$, allyl

[a] Reagents and conditions: i, R^5_3MnM (M = Li, MgBr), THF, 0 °C; ii, H_2O.

in the presence of a catalytic amount of manganese(II) chloride.

Alkyl halides were reduced to the corresponding alkanes by the homonuclear bridging hydride (μ-H)-$[(\eta^5\text{-MeCp})Mn(CO)_2]_2^-PPN^+$ [PPN = bis(triphenylphosphoranylidene)ammonium] in THF at 40−60 °C under pseudo-first-order reaction conditions, where an excess of alkyl halide was employed under a nitrogen atmosphere.[200] The reaction was of overall second-order, first-order with respect to the bridging hydride and first-order respect to the alkyl halide, the complex $(\eta^5\text{-MeCp})Mn(CO)_3$, PPN^+X^-, and the alkane being the major products. The kinetic and ESR data, together with the reaction with cyclopropyl carbinyl bromide (giving rise to methylcyclopropane and 1-butene) ensure that two possible pathways are operable in this reaction: (a) a concerted mechanism involving hydride transfer; (b) a single-electron-transfer mechanism.

2. Rhenium

Hydrogenation of 6- and 7-alkyl-2-(4′-bromophenyl)indolizines over rhenium heptasulfide proceeded with hydrodebromination, leading to mixtures of *cis*- and *trans*-isomers of 6- and 7-alkyl-2-phenylindolizidines.[201]

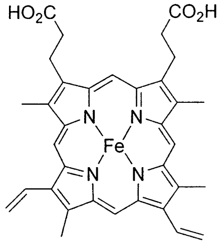
E. Group VIIIB. First Triad: Fe, Co, Ni

1. Iron

Iron is without any doubt one of the most studied transition metals in the hydrodehalogenation of organic halides, above all in the zerovalent state, a topic to which we will dedicate most of this section. Nevertheless, we will start covering some of the reports in which other forms of iron, such as iron complexes and salts, have been utilized in reducing systems. For instance, a novel reducing system was discovered in the early 1990s by Voronkov et al. based on triethylsilane and catalytic amounts of iron(III) acetylacetonate (0.15 mol %).[202] This combination found application in the reduction of aromatic monocarboxylic acid halides (ArCOCl, Ar = Ph, 2-BrC_6H_4, 2,4-$Br_2C_6H_3$) to the corresponding aldehydes at 20 °C for 20 min. Although conversions were around 90%, isolated yields of benzaldehyde were rather low. Alkylmagnesium halides in the presence of catalytic amounts of iron(III) acetylacetonate reduced several 1,1-dibromo-2-aryl-1-alkenes to afford the corresponding (*E*)-1-bromo-1-alkenes in good yields and excellent stereoselectivity.[203]

Reductive dehalogenation has been shown to be mediated by transition-metal macrocycles such as hematin, coenzyme F_{430}, and cobalamin. These macrocycles along with several other biomimetic complexes have been studied in homogeneous abiotic aqueous systems as potential remediation catalysts for biomimetic reductive dehalogenation of halogenated hydrocarbons.[204] These abiotic but biomimetic systems have provided information on possible dechlorination mechanisms of chlorinated aliphatics and aromatics with greatly enhanced reaction rates over those of in vivo systems.

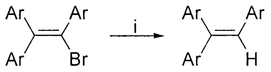
The transition-metal coenzyme hematin (**190**) was reported to catalyze the reductive dechlorination of polychlorinated ethylenes and benzenes, using titanium(III) citrate or dithiothreitol ($HSCH_2CHOHCHOHCH_2SH$) as reductant, whereas the electron-transfer proteins four-iron ferredoxin, two-iron ferredoxin, and azurin (Cu) were inactive.[205] For hematin, the order of reductive dechlorination rates was carbon tetrachloride > hexachlorobenzene > tetrachloethylene, regio- and stereospecific reactions also being observed. For instance, *cis*-1,2-dichloroethylene was the predominant product formed in the reductive dechlorination of trichloroethylene. Furthermore, hematin was demonstrated to dechlorinate tetrachloroethylene to vinyl chloride, but also catalyzed the dehalogenation of hexachlorobenzene (to pentachlorobenzene), and *meta*- and *para*-dechlorination (with respect to the nonchlorinated carbon) of pentachlorobenzene. In general, hematin had slower chloroethylene dechlorination kinetics than vitamin B_{12} and coenzyme F_{430}, within each class of compounds (alkane, alkene, and benzene) the rates of dechlorination decreasing with decreasing chlorine content. A reaction mechanism for the transformation of carbon tetrachloride into chloroform by hematin in aqueous titanium(III) citrate medium was proposed.[206]



190

A number of triarylvinyl halides **191** were reduced to the corresponding alkenes **192** with LAH using iron(II) chloride or nickel(II) chloride as catalyst (Scheme 68).[207] The reduction was suggested to take

Scheme 68[a]



191 **192**

(90-96%)

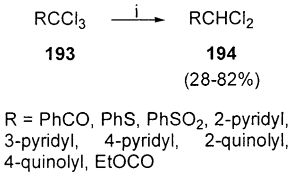
Ar = Ph, p-Tol, An

[a] Reagents and conditions: i, LAH, $FeCl_2$, THF, 5−15 min.

place via an initial electron-transfer process or metalation reaction. A direct S_N2 displacement was ruled out since starting from either an (*E*)- or (*Z*)-isomer afforded the (*E*)- and (*Z*)-alkenes in equimolar amounts. The reduction of ^{13}C-labeled starting materials did not result in any scrambling of the label from C-2 to C-1, thus indicating that no rearrangement occurred during the reaction.

The reductive electron transfer of a series of trichloromethyl derivatives **193** was induced by iron(II) chloride, to give as the main reaction products the homocoupling dimer ($RCCl_2-CCl_2R$) and the hydrodehalogenated derivatives **194** (Scheme 69).[208]

Scheme 69[a]



[a] Reagents and conditions: i, $FeCl_2 \cdot 4H_2O$, MeCN, 25 °C (or 80 °C), 7−48 h.

As a general rule, **194** are the major products when the R group contains substituents which make further reduction of the radical to the carbanion easier, and behave as ligands toward the iron(II) ion. In the other cases, the dimer $RCCl_2-CCl_2R$ is the main product. Thus, molecules containing carbanion-stabilizing groups in the R moiety are likely to be involved in halogen−hydrogen exchange. When groups with lower α-carbanion-stabilizing ability are involved, the activation energy required for both processes can be virtually identical, although increasing the iron(II):substrate molar ratio seemed to promote hydrodehalogenation with respect to the dehalocoupling.

Iron(II) chloride,[209a] as well as iron oxides,[209b,c] is also known to promote dehydrochlorination of organic chlorides instead of hydrodechlorination. A fresh-ground anaerobic pyrite system was found to transform carbon tetrachloride into chloroform at room temperature in approximately 50% yield.[210] On the other hand, the use of zerovalent transition metals, and in particular of iron metal, to degrade halogenated contaminants, represents an active research area and one of the latest technologies for environmental remediation.[211] Therefore, as mentioned at the beginning of this section, from this point we will deal exclusively with iron in the zerovalent state as reducing agent.

Reduction of chlorinated solvents by fine-grained iron metal was studied by Tratnyek et al. in well-mixed anaerobic batch systems to help assess the utility of this reaction in remediation of contaminated groundwater. Iron was found to dehalogenate sequentially carbon tetrachloride, via chloroform, to methylene chloride.[212a] The initial rate of each reaction step was pseudo-first-order in substrate and became substantially slower with each dehalogenation step. Thus, carbon tetrachloride degradation typically occurred in several hours, but no significant reduction of methylene chloride was observed over one month. This reductive dehalogenation did not lead to chloromethane, methane, or coupling products such as hexachloroethane. Trichloroethylene (TCE) was also dechlorinated by iron, although more slowly than carbon tetrachloride. Increasing the clean surface area of iron greatly increased the rate of carbon tetrachloride dehalogenation, whereas increasing pH decreased the reduction rate slightly. The kinetics of all these reactions was deeply studied.[212b−g] Similar experiments on the dechlorination of carbon tetrachloride to chloroform and methylene chloride by elemental iron were studied by other groups.[213]

Elemental iron reduced part-per-thousand levels of aqueous-phase carbon tetrachloride to chloroform in a few hours.[214] Free metal ions, chloride ion, and hydrogen gas were produced in the reaction, process kinetics being dependent on the solution pH, surface area of the elemental metal, carbon tetrachloride concentration, buffer selection, and solvent composition. The reaction rate was first-order with respect to carbon tetrachloride at concentrations less than 7.5 mM. Transformation rates were significantly greater in comparison with the use of elemental zinc (see section VI.I). Degradation of carbon tetrachloride by iron was found to be accelerated by the presence of sulfur-containing compounds such as sodium sulfate, sodium sulfide, iron sulfide, iron disulfide, and an organosulfonic acid.[215]

Zerovalent iron powder was reported to hydrodehalogenate 1,2-dibromo-3-chloropropane (DBCP) to propane under water treatment conditions (ambient temperature and circumneutral pH).[216] DBCP reacted with iron powder (100−200 mesh) in buffered water (pH 7) with a half-life of 2.5 min, and in different groundwaters (pH 8.2−8.7) with a half-life ranging from 41 to 77 min. Dissolved oxygen and nitrate slowed the transformation, whereas sulfate and nitrite had little effect. A comparison of the catalyst with a palladium on alumina catalyst under hydrogen was established.

Dechlorination of chlorinated ethenes is one of the most studied processes due to their extensive use in industry and consequently their common occurrence in groundwater, showing a high resistance to both biotic and abiotic degradation under natural subsurface conditions. Iron has been demonstrated to be an excellent reducing agent for the destruction of these contaminants.[211d,217] In this context, Gillham et al. conducted a series of flow-through column tests to investigate the products of degradation of aqueous TCE in contact with granular iron metal.[218] The results indicated the degradation process to be pseudo-first-order over the initial concentration range of 1.3−61 mg/L TCE, the mean half-life for TCE being 3.25 h. Thus, the rates of degradation are remarkably fast compared to natural rates of abiotic degradation. The principal degradation products were ethylene, followed by ethane with substantially smaller amounts of other C_1-C_4 hydrocarbons. On the basis of the low concentrations of chlorinated degradation products in the solution phase (3.0−3.5%), it was proposed that most of the TCE remained sorbed to the iron surface until complete dechlorination was achieved. The mechanism remained uncertain since although electron transfer and dechlorination mechanistically might proceed sequentially on the iron surface, the small proportion of chlorinated intermediates and their simultaneous appearance in the solution phase argued against sequential dechlorination.

The effect of concentration, initial pH, metal loading, and the particle size of the metal were studied in the degradation of TCE using zerovalent iron.[219] The degradation rate was found to be first-order with respect to TCE, the conversion being independent of the initial TCE concentration. The amount of TCE degraded at any given time was directly proportional to the dissolved iron in solution, the metal surface area playing a crucial role in the process. A 2-fold increase in the pseudo-first-order rate was obtained when the metal particle size was decreased from 370 μm by a factor of 2.5.

Zang et al. reported an efficient method of synthesizing nanoscale (1−100 nm) iron and palladized iron particles (the latter will be tackled with more detail below), useful for the transformation of TCE and PCBs.[220] TCE was completely dechlorinated by synthesized nanoscale Fe particles within 1.7 h, the final reaction products in the headspace of nanoscale particle solutions being identified as hydrocarbons, including ethylene, ethane, propylene, butene, butane, and pentane. Arochlor 1254 was partially dechlorinated (<25%) within 17 h by the nanoscale Fe particles at ambient temperature with accumulation of biphenyl in the solution, whereas little degradation was observed with the commercial iron powders under the same experimental conditions.

A generalized kinetic model was developed by Bhattacharyya et al. for two-phase systems involving reactions in one phase with product partitioning into a second phase, and applied to the reductive dehalogenation of TCE with zerovalent iron.[221a] Sorption effects were included to incorporate the partitioning onto the solid. Likewise, a new parameter, the “fractional active site concentration”, was introduced to incorporate the differences in reactive and nonreactive sites on the iron surface, which affects the degradation performance. The model predictions were verified with the experimental data and the results from the literature. The same research group employed surface characterization techniques to gain insight into the metallic surface effects involved in the reductive dehalogenation of TCE with zerovalent iron.[221b] It was found that the defects present on the surface acted as reactive sites for the dehalogenation process. A simple way to increase the number of abnormalities on the surface was by chloride pretreatment, thus causing improvement in the degradation rates at early times. On the other hand, these enhancements disappeared at longer reaction times, which was attributed to the decrease in the surface roughness over the course of the reaction. The increased reaction rates were attributed to the morphological changes occurring on the surface of iron, which were studied by surface profilometry and atomic force microscopy (AFM).

Halogenated solvents from different sources are thought to have a unique isotopic composition, and this can be used to trace pollutants to their sources.[222] Such an approach is premised on the assumption that no alteration of the isotopic compositions occurs from the time of contaminant release to the time of sample collection. However, numerous physical and biological processes involving the organic contaminant of interest could affect the isotopic composition. By understanding the extent of fractionation in reactions such as reductive dehalogenation, the type and extent of reactions of chlorinated ethenes could be understood retroactively in natural and engineered systems. The magnitude and direction of the carbon isotopic fractionation of chlorinated ethenes TCE, tetrachloroethylene, and 1,2-*cis*-dichloroethylene were determined during dehalogenation by metallic iron.[223] Compound-specific isotopic analysis showed large isotopic deviations during the reaction duration for each of the solvents, with ^{13}C shifts of 24‰, 12‰, and 24‰, respectively, after 80−90% consumption. The fact that these large changes in isotopic composition can occur during reductive dehalogenation has significant implications for monitoring the progress of zerovalent iron remediation. Thus, if chlorinated ethenes from contaminated sites can be analyzed for carbon isotope composition at any given point of a remediation program, the above results indicate that the efficacy of remediation can be assessed quantitatively.

The effects of pH on dechlorination of TCE by zerovalent iron were also studied by others.[224] The rate constant of TCE linearly decreased between pH 3.8 and 8.0, whereas at pH 1.7 it was more than an order higher than that at pH 3.8. Degradation of TCE was not observed at pH values of 9 and 10, the optimal rate being achieved at pH 4.9. As the rate of iron corrosion was significantly high at pH 1.7 and 3.8, it was suggested that lowering the solution pH might not expedite the degradation rate of TCE by zerovalent iron as it also caused faster disappearance of iron, and hence decreased the zerovalent iron surface concentration.

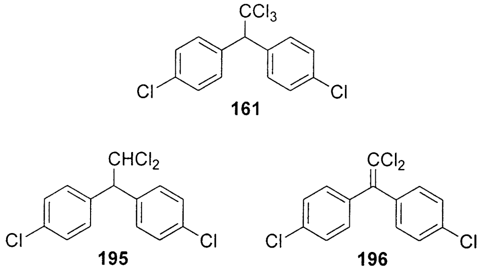
Enhanced solubilization and destruction of tetrachloroethylene in water by hydroxypropyl-β-cyclodextrin (HP-β-CD) and iron was observed by Reynolds et al. both in static and in flowing systems.[225] In flowing systems, metallic iron completely removed tetrachloroethylene, no other chlorinated ethylene species being detected in the column effluent. The solubility enhancement and reaction with metallic iron were consistent with reversible formation of a stoichiometric HP-β-CD−tetrachloroethylene complex. The sorption, pathways, and kinetics in the reduction of chlorinated ethenes by the metallic iron−water system were widely studied by Burris, Roberts, et al.[226]

Besides the above-mentioned chlorinated solvents, other halogenated organic materials have also been subjected to dehalogenation by zerovalent iron. For instance, zerovalent iron promoted the dechlorination of PCBs (Arochlor 1221) in the absence of solvent in a high-temperature environment.[227] Most of the PCBs were dechlorinated to biphenyl within 10 min at 400 °C, the latter being stable at that temperature. At temperatures higher than 500 °C, dechlorination and other reactions of PCBs occurred. Water appeared to be the hydrogen donor for the formation of biphenyl, as shown by an experiment with added deuterium oxide.

PCBs Arochlor 1242 and 1248 were also efficiently dechlorinated (but not quantitatively) with heated columns of zerovalent metals or bimetallic mixtures in supercritical carbon dioxide and in a continuous process.[228] The extent of dechlorination was dependent on the zerovalent metal (Fe > Ni > Zn > Cu), temperature (400 ≫ 300 > 200 °C), and pressure (≤4500 psi). The inclusion of a methyl ketone in the feedstock solution appreciably improved the extent of dechlorination.

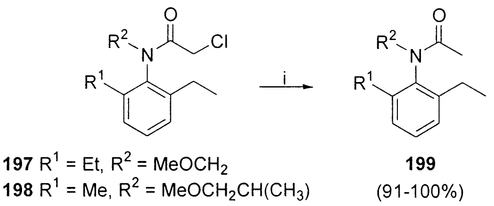
The capability of powdered zerovalent iron to dechlorinate DDT and related compounds at room temperature was investigated by Sayles et al.[229] Specifically, DDT (**161**), DDD [1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane] (**195**), and DDE [1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene] (**196**) were successfully dechlorinated by powdered zerovalent iron in buffered anaerobic aqueous solution at 20 °C, with or without the presence of nonionic surfactant Triton X-114 (Chart 17). The rates of dechlorination of DDT and DDE were independent of the amount of iron, with or without surfactant, though rates with surfactant were much higher than without. A mechanistic model was constructed that quantitatively fits the observed kinetic data, indicating that the rate of dechlorination of the solid-phase reactants was limited by the rate of dissolution into the aqueous phase.

Chart 17. Reductive Dechlorination of DDT, DDD, and DDE by Powdered Fe at 20 °C in Buffered Anaerobic Aqueous Solution with or without Triton X-114



Granular iron metal was found to cause the reductive dechlorination of two important chloracetanilide herbicides, alachlor (**197**) and metolachlor (**198**),[230] used for broadleaf weeds and annual grasses in domestic soybean and corn crops. The reaction was performed with granular cast iron in aqueous solutions at room temperature. A two-site, rate-limited sorption and first-order degradation model was applied to both batch data sets, with excellent agreement for alachlor and fair agreement for metholachlor. The products of the reaction were chloride ion (84% mass balance for alachlor and 68% for metholachlor) and the corresponding dechlorinated acetanilides (**199**) (Scheme 70). The *N*-dealkylated acetanilide was a minor byproduct (9%) in the case of alachlor.

Scheme 70[a]

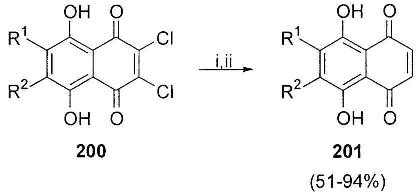


197 R^1 = Et, R^2 = $MeOCH_2$
198 R^1 = Me, R^2 = $MeOCH_2CH(CH_3)$

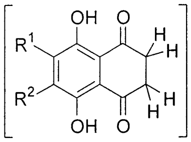
[a] Reagents and conditions: i, Fe (40 mesh), H_2O, rt, 5 d.

The naphthazarin and quinizarin moieties are widely distributed in nature, but also present in several pharmacologically active compounds, therefore being useful precursors for their syntheses.[231] A series of naphthazarins **201** and an example of quinizarin (**201**, R^1-R^2 = fused benzene) were straightly synthesized from the corresponding 2,3-dichloronaphthazarins and quinizarin **200**, the key step of the synthesis being the reductive dehalogenation promoted by iron in refluxing glacial acetic acid, followed by oxidation with air (Scheme 71).[232]

Scheme 71[a]



R^1 = H, Me, Et, n-$C_{15}H_{31}$, $(CH_2)_3CO_2H$, Cl
R^2 = H, Me, Bu^t, Cl, Bu^nNH, OH, OEt, tetra-*O*-acetyl-β-D-glucopyranosyloxy
R^1-R^2 = fused benzene



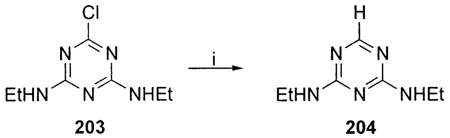
202

[a] Reagents and conditions: i, Fe (powder), HOAc, reflux, 3−50 min; ii, 5% NaOH, air.

The reaction took place through the intermediate dihydro derivatives **202**.

Atrazine (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine) (**203**) is a herbicide used extensively in corn, sorghum, and sugarcane fields for the last 30 years,[233] with a long half-life in the environment (up to one year).[234] The possible water contamination, combined with the uncertainty of atrazine's carcinogenic and toxicological effects, has spurred interest in techniques that might more rapidly degrade atrazine and its metabolites. Batch aqueous experiments using fine-grained (100 mesh) zerovalent iron as an electron donor resulted in reductive dechlorination of atrazine to give 2-ethylamino-4-isopropylamino-1,3,5-triazine (**204**) (Scheme 72).[235] Identification of this compound initiated the development of analytical methods using HPLC, GC/MS, and HPLC/MS, to

Scheme 72[a]



[a] Reagents and conditions: i, Fe (100 mesh), H_2O, 23 °C.

simultaneously quantify atrazine (**203**) and dechlorinated atrazine (**204**).

The dechlorination of atrazine (**203**) with metallic iron under low-oxygen conditions was studied at different reaction mixture pH values (2.0, 3.0, and 3.8).[236] The pH control was achieved by addition of sulfuric acid throughout the duration of the reaction. The lower the pH of the reaction, the faster the degradation of atrazine. The observed products of the degradation reaction were dechlorinated atrazine (**204**) and possibly hydroxyatrazine (2-ethylamino-4-isopropylamino-6-hydroxy-1,3,5-triazine). Triazine ring protonation was proposed to account, at least in part, for the observed effect of pH on atrazine by metallic iron.

Although the mechanisms of these reductions with zerovalent iron are not well elucidated, it appears that, generally, a two-electron transfer occurs either directly at the iron surface (by absorption of the organic halide) or through some intermediary [Scheme 73, (1)].[237] In a different mechanistic context, numerous studies have shown that dissociative adsorption of water takes place at clean iron metal surfaces, resulting in surface-bound hydroxyl, atomic oxygen, and atomic hydrogen ("nascent hydrogen").[238] The latter species can combine with itself, accounting for the formation of molecular hydrogen, or react with other compounds in the system, resulting in their hydrogenation [Scheme 73, (2) and (3)]. A third possibility would be the reduction by iron(II), resulting from corrosion of the metal [Scheme 73, (4)]. A debate over the relative importance of these mechanisms[212] has gone on for many years, but the electron-transfer model is generally preferred.

Scheme 73

$$RX + Fe^0 + H^+ \longrightarrow RH + Fe^{2+} + X^- \quad (1)$$

$$Fe^0 + 2H_2O \rightleftharpoons Fe^{2+} + H_2 + 2OH^- \quad (2)$$

$$RX + H_2 \longrightarrow RH + H^+ + X^- \quad (3)$$

$$RX + 2Fe^{2+} + H^+ \longrightarrow RH + 2Fe^{3+} + X^- \quad (4)$$

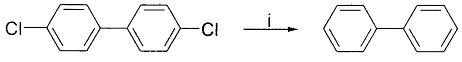
Other combinations of iron metal were also effective in the hydrodehalogenation of organic halides. For instance, galvanized steel sheet and stainless steel tubing (aluminum tubing was also studied) were exposed to water and for periods of five weeks to low concentrations of the following halogenated hydrocarbons: 1,1,1-trichloroethane, 1,1,2,2-tetrachloroethane, hexachloroethane, bromoform, and tetrachloroethylene.[239] Stainless steel was found to be the least reactive metal, causing depletion of only two compounds, bromoform and hexachloroethane, the depletion being substantial, however, amounting to 70% after 5 weeks. Aluminum caused reductions greater than or equal to 90% for all compounds except for tetrachloroethylene, whereas galvanized steel caused depletion greater than or equal to 99% for all compounds. Thus, the halogenated compound disappearance rates decreased in the order galvanized steel > aluminum > stainless steel. The order in which the compounds disappeared was bromoform > hexachloroethane > 1,1,1-trichloroethane > 1,1,2,2-tetrachloroethane > tetrachloroethylene. The reduction of halocarbon concentrations by the metals was believed to occur by reductive hydrogenolysis involving the metal surface or metal ions released from the surface. Halocarbon concentrations declined rapidly after an initial delay period, the more halogenated compounds generally being removed before the less halogenated compounds, since the latter were also generated by reductive hydrogenolysis of the former. The fact that stainless steel showed the lowest activity was probably due to the fact that it is the most inert with respect to corrosion. However, a steel batch reactor was effective in the hydrodechlorination of 1-chlorohexadecane and 2-chloronaphthalene in water under supercritical conditions.[240] Reactions were carried out at 275−430 °C under nitrogen, hydrogen evolved from the reaction of HCl with the metal wall of the reactor participating in the process.

2. Cobalt

The combination developed by Voronkov et al. based on triethylsilane and iron acetylacetonate, previously mentioned, also found application with cobalt(III) acetylacetonate to the reduction of aromatic monocarboxylic acid halides to the corresponding aldehydes (see iron).[202]

Catalytic amounts of cobalt(II) acetylacetonate were used by Vcelak et al. to accelerate the reduction of several polychlorinated aromatics by the reagent dihydridobis(2-methoxyethoxy)aluminate (SDMA).[90b] Thus, the reduction of 4,4′-dichlorobiphenyl was accelerated by ca. 2 orders of magnitude in the first step (monodechlorination) and somewhat less in the second step, compared to the noncatalyzed reaction. Comparing Co(acac)$_2$ with Ni(acac)$_2$, the former showed higher efficiency for total dechlorination [e.g., 4,4′-dichlorobiphenyl (**205**) was transformed into biphenyl (**20**) in 84% yield at 70 °C for 1 h and 98% yield at 110 °C with reused catalyst (Scheme 74)], whereas the latter was more selective and appropriate for monodechlorination.

Scheme 74[a]

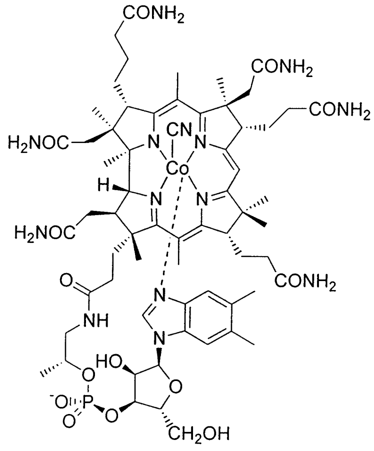


205 **20**
(84-98%)

[a] Reagents and conditions: i, SDMA, Co(acac)$_2$ (5 mol %), PhMe, 70−110 °C, 1 h.

A more detailed study covering the reaction of SMDA with other metal acetylacetonates and palladium derivatives, using 1,4-dichlorobenzene and chlorobenzene as model substrates, revealed the following decreasing order in catalytic effect: Co ≈ Ni ≈ Pd > Cu ≫ Mn > Fe.[241a] The dehalogenation reaction was well described by a kinetic model consisting of the set of dehalogenation steps, which were first-order in the chloroarene combined with the catalyst deactivation, and second-order in the transition-metal compound. As a direct application, SDMA in the presence of catalytic amounts of cobalt(II) acetylacetonate caused the complete dechlorination of PCB Delor 103 (42.6% Cl).[241b] The high conversion (over 99.5%) to biphenyl was achieved at 110 °C in short reaction times (less than 60 min). Co(acac)$_2$ was more efficient than Ni(acac)$_2$ for the dechlorination at 70 °C, while the efficiencies of both were comparable at higher temperatures.

The hematin-catalyzed reductive dechlorination of polychlorinated ethylenes and benzenes, reported by Wackett et al., was extended to other transition-metal coenzymes such as vitamin B$_{12}$ (**206**).[205] In this case, the reductive dechlorination rates for different classes of perchlorinated compounds followed the order carbon tetrachloride > tetrachloethylene > hexachlorobenzene. Vitamin B$_{12}$ was capable of sequentially dechlorinating tetrachloroethylene to ethylene, pentachlorobenzene, and pentachlorophenol, yielding two out of three possible isomeric tetrachlorobenzenes. Reductive dechlorination of (2,4,5-trichlorophenoxy)acetic acid was also described. Other general trends were similar to those previously commented on for hematin. Further work on the reduction of polychlorinated ethanes with vitamin B$_{12}$ and titanium(III) citrate was carried out.[242] Hexachloroethane, pentachloroethane, 1,1,1,2-tetrachloroethane, and 1,1,2,2-tetrachloroethane gave mainly the products of reductive elimination tetrachloroethylene, trichloroethylene, 1,1-dichloroethylene, and *cis*- and *trans*-dichloroethylene, respectively. However, when chlorine atoms were present on one carbon only, a strictly reductive pathway of dechlorination was observed. Thus, 1,1,1-trichloroethylene was transformed sequentially to 1,1-dichloroethane, chloroethane, and ethane.



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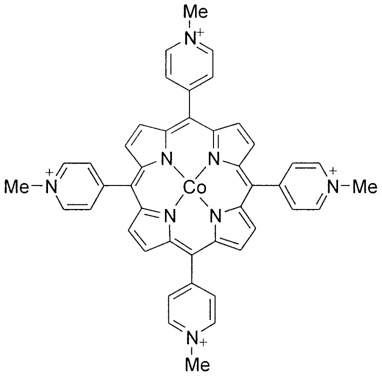
The metallocoenzyme-mediated reductive dechlorination of carbon tetrachloride has attracted the attention of several research groups. For instance, Vogel et al. presented a mechanistic study on the reductive dechlorination of carbon tetrachloride by vitamin B$_{12}$ (cyanocobalamin) (**206**) in the presence of dithiothreitol as a function of the redox potential and pH.[243] The chemical control of the redox potential was achieved by changing the reducing agent concentration and the pH, the former decreasing when both the total concentration of dithiothreitol and pH increased. The pseudo-first-order rate constant of carbon tetrachloride disappearance increased with decreasing redox potential. The predominant cobalt species under the reaction conditions was found to be cobalamin(II), suggesting a one-electron reduction of vitamin B$_{12}$ and the involvement of two vitamin B$_{12}$ molecules per reacting carbon tetrachloride molecule. A reaction pathway was proposed for this carbon tetrachloride reduction to chloroform, the participation of Co(II) in these reductive dechlorination reactions being demonstrated.

Another pathway for the reductive transformation of carbon tetrachloride catalyzed by vitamin B$_{12}$ in aqueous titanium(III) citrate solution was proposed on the basis of spectroscopic, kinetic, and isotopic studies.[206] The reaction was zero-order in carbon tetrachloride and first-order in vitamin B$_{12}$, the proposed rate-limiting step being the reduction of the stable trichloromethylcobalamin intermediate (CCl_3−Cbl) by titanium(III) citrate at alkaline pH and the sterically induced CCl_3−Cbl decomposition at neutral pH. In comparison with hematin, vitamin B$_{12}$ was shown to be a more stable and more effective catalyst. Chloroform was the primary product obtained, and the yield was a function of pH, Ti(III) concentration, and organic content, titanium(III) citrate controlling the transformation rate and the chloroform formation. Alternatively, cysteine was used as reductant instead of titanium(III) citrate, a vitamin B$_{12}$ (reduced form)−cysteinate complex being proposed as the reactive species.[244]

Carbon tetrachloride was used as a model compound to study its reductive dehalogenation in aqueous systems, mediated by nonspecific biomimetic cobalt macrocycles.[245] Two water-soluble macrocycles, cobalt tetrakis(*N*-methyl-4-pyridiniumyl)porphyrin (CoTMPyP) cation (**207**) and cobalt tetrasulfophthalocyanine (CoPcTs) anion (**208**), were used as homogeneous and mineral-supported catalysts[246] (Chart 18). The supported catalysts were prepared by exchanging CoTMPyP on the hectorite, fluorohectorite, and amorphous silica surface, and by exchanging CoPcTs on the layered double hydroxide surface. The

Chart 18. Structure of CoTMPyP Cation and CoPcTs Anion



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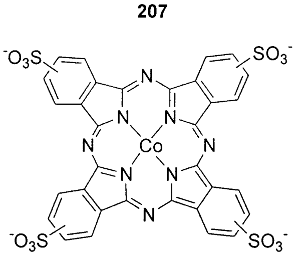

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supported macrocycles were catalytically active, the heterogeneous dechlorination reactions being described by rate constants correlated to the accessibility and hydration of the cobalt in the supported macrocycles, following the order CoTMPyP−silica > CoPcTs-layered double hydroxide > CoTMPyP−fluorohectorite > CoTMPyP−hectorite. In short-term experiments (2 h), homogeneous CoTMPyP was more active than heterogeneous catalysts, while homogeneous CoPcTs was deactivated due to aggregation, and degraded less carbon tetrachloride than supported CoPcTs. However, in long-term experiments (3 d), where large carbon tetrachloride:macrocycle ratios were used, silica-supported CoTMPyP was more active than homogeneous CoTMPyP, suggesting that adsorption stabilized the catalyst. Chloroform and dichloromethane were detected as the degradation products in the homogeneous systems, whereas only chloroform was detected in the heterogeneous systems.

A comparative product analysis was also reported for the carbon tetrachloride dehalogenation catalyzed by cobalt corrins (vitamin B_{12}, cobinamide dicyanide, or aquocobalamin) and a reductant [titanium(III) citrate, dithiothreitol, or sulfide−cysteine].[247] Products in the presence of titanium(III) citrate, which yielded the Co(I) form of the corrin, were mostly hydrogenolytic products and included predominantly methyl chloride and methane. Thiol reducing agents, which led to the Co(II) form of the corrin, yielded more highly halogenated products including dichloromethane, carbon monoxide, and formate, in the case of dithiothreitol. Sulfide−cysteine reductants were the least effective, with the major products identified being chloroform, carbon disulfide, 2-oxothiazolidinecarboxylic acid, and 2-thioxo-4-thiazolidinecarboxylic acid. A reaction mechanism was proposed involving the formation of a trichloromethyl radical, which forms an adduct with the reductant and, in the case of sulfide−cysteine, ultimately produces carbon disulfide or thiazolidines by way of thiophosgene. Alternatively, the radical can be further reduced to form chloroform and dichloromethane or carbon monoxide and formate through a dichlorocarbene intermediate.

It was shown that, in homogeneous aqueous solution containing titanium(III) citrate or titanium(III)−nitrilotriacetic acid as bulk electron donors, cobalamin, cobinamin, and cobamin were effective electron-transfer mediators for the reduction of tetrachloroethylene, TCE, and trichlorofluoroethylene.[248] For a given chlorinated ethene, the reaction rate varied only slightly with the pH and type of corrinoid present, and was about 5 and 50 times faster for tetrachloroethylene as compared to trichlorofluoroethylene and TCE, respectively. The product distribution of the reduction of TCE at pH 7−9 was acetylene (4−7%), ethylene (2−25%), *cis*-1,2-dichloroethylene (63−72%), and *trans*-1,2-dichloroethylene (4−6%). The product distribution of the reduction of trichlorofluoroethylene at pH 7−9 was 1,1-dichlorofluoroethylene (12%), *cis*-dichlorofluoroethylene (73%), and *trans*-dichlorofluoroethylene (15%). Evidence was presented that the first and rate-limiting step of all substrates was a dissociative one-electron transfer, yielding the corresponding vinyl radicals. Furthermore, the elimination of a chloride radical from the 1,1-dichlorovinyl radical, yielding chloroacetylene and subsequently acetylene, was proposed to account for the direct formation of acetylene out of TCE.

Burris et al. also studied the reduction of tetrachloroethylene and TCE catalyzed by vitamin B_{12} in both homogeneous and heterogeneous (vitamin B_{12} bound to agarose) batch systems using titanium(III) citrate as the bulk reductant. The reaction rates proved to be comparable in both cases, no loss in tetrachloroethylene reducing activity being observed with repeated usage of the heterogeneous catalyst.[249a] A kinetic model, incorporating substrate−vitamin B_{12} electron-transfer complex formation and subsequent product release, was developed by Burris et al., for the vitamin B_{12}-catalyzed reductive dechlorination of tetrachloroethylene using titanium(III) citrate as the bulk reductant.[249b]

The vitamin B_{12}–titanium(III) citrate system was also applied to the reductive transformation of chloroacetylene (to acetylene and vinyl chloride), 1,1-dichloroethene (to a wide range of products), and *cis*- and *trans*-dichloroethene (to vinyl chloride, ethylene, and ethane) at pH 8 and 22 °C.[250]

Vitamin B_{12} catalyzed the chemical reduction of other substrates, such as the allylic halides geranyl bromide and methyl (2*E*,6*E*)-8-bromo-3,7-dimethyl-2,6-octadienoate.[251] The formation and distribution of the reaction products were explained by free radical mechanisms, namely, by reductive reactions of functional groups, rearrangements, and intermolecular coupling of radical intermediates.

The Co(I) form of vitamin B_{12} [cob(I)alamin)] has been electrocatalytically generated from the Co(II) form of vitamin B_{12}, and applied by Rusling et al. to the dehalogenation of α-haloacetic acids.[252a] Dehalogenation of chloroacetic acid, trichloroacetic acid, and bromoacetic acid to acetic acid by cob(I)alamin was spontaneous, regeneration of cob(II)alamin taking place at the electrode. The experiments confirmed that the predominant reaction was the two-electron cleavage of the carbon−halogen bond. The rate-determining step was assumed to be the reaction of cob(I)alamin with the haloacid [Scheme 75, (2)], the R^- presumably undergoing protonation in the weakly acidic reaction medium. It was also observed that the more easily reduced trichloroacetic acid gave a rate constant about 25 times larger than that of chloroacetic acid, the rate constant for bromoacetic acid being similar to that of trichloroacetic acid but 15-fold larger than that of chloroacetic acid. Electrogenerated Co(I) macrocycles $Co^{I}L$ derived from vitamin B_{12}, complex **208** (Chart 18), and Co(salen) were also used in bicontinuous microemulsions made from dodecane, water, and didodecyldimethylammonium

Scheme 75

$$\mathrm{Co(II)} + e^- \rightleftharpoons \mathrm{Co(I)}\ \text{(at electrode)}\quad (1)$$

$$\mathrm{Co(I)} + \mathrm{RX} \longrightarrow \mathrm{R}^{\bullet} + \mathrm{Co(II)} + \mathrm{X}^- \quad (2)$$

$$\mathrm{Co(I)} + \mathrm{R}^{\bullet} \longrightarrow \mathrm{R}^- + \mathrm{Co(II)}\ \text{(fast)}\quad (3)$$

bromide, for the reduction of *n*-alkyl bromides (RBr's) through the corresponding S_N2 complexes $R-Co^{III}L$.[252b]

Recent studies on heterogenizing homogeneous transition-metal catalysts revealed that physical entrapment of metallic complexes in SiO_2–sol–gel matrixes permits facile recycling of the encapsulated catalysts, but also an enhancement of their stability and catalytic properties.[253a] Thus, the heteronuclear complex $Rh_2Co_2(CO)_{12}$, physically entrapped in SiO_2–sol–gel matrixes, was utilized as a recyclable catalyst in the hydrogenolysis of 1-chloronaphthalene (3.4 atm of H_2, 30 °C, 22 h), to give mainly the overreduced products *cis*- and *trans*-decalin (82% and 12%, respectively).[253b]

Hydrogenolysis of neopentyl iodide was accomplished on cobalt dispersed on a magnesium oxide support, the main product at 70 °C being neopentane (>96%).[254] 2-Methylbutane and 2-methylbutenes were also obtained above all at higher temperatures (≥100° C). A π-complex-based mechanism was suggested to be involved in the activation of the carbon–iodine bond and in the evident 1,2-methyl shift. Cobalt supported on alumina catalysts was also reported to promote hydrodechlorination of 1,2-dichloroethane and chlorobenzene at 400–600 °C in the presence of hydrogen.[255]

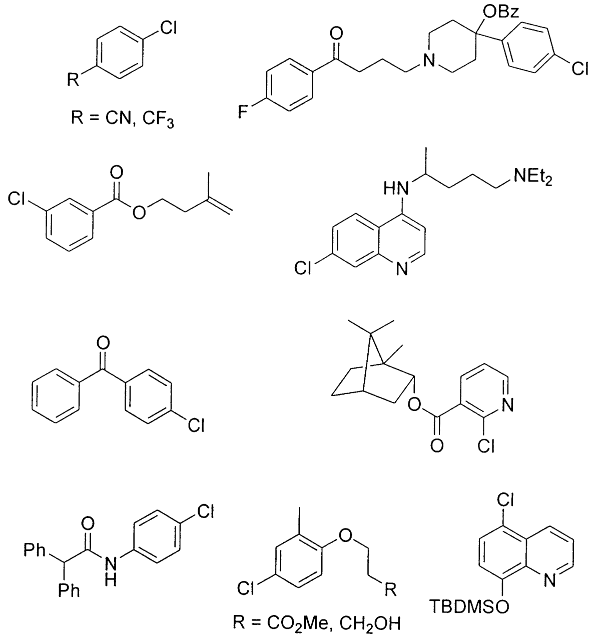
3. Nickel

Dehalogenation mediated by homogeneous nickel complexes has been reported by different groups. For instance, nickel(III) acetylacetonate in combination with triethylsilane showed similar behavior compared to iron(III) and cobalt(III) acetylacetonates in the reduction of aromatic monocarboxylic acid halides to the corresponding aldehydes (see iron and cobalt).[202] Catalytic amounts of nickel(II) acetylacetonate (as well as cobalt acetylacetonate) also accelerated the dehalogenation of 4,4′-dichlorobiphenyl with SDMA.[90b]

The hydrodehalogenation of 1,2,3-trichlorobenzene with sodium borohydride and the catalytic system formed by $(Ph_3P)_2NiCl_2$ in the presence of free phosphine was accomplished in different solvents.[256] High dechlorination rates were obtained using ethanol–pyridine mixtures, the presence of an excess of phosphine increasing the stability of the system and the highest activity being obtained for a 2:1 phosphine:$NiCl_2(Ph_3P)_2$ ratio.

Lipshutz et al. recently described a mild and selective reduction of aryl halides catalyzed by low-valent nickel complexes, which were generated by the combination of reagents $(Ph_3P)_2NiCl_2$, Ph_3P, $Me_2NH\cdot BH_3$, and K_2CO_3 (or Cs_2CO_3) in CH_3CN.[257] Many functional groups were compatible with these reaction conditions, including aryl ketones, aryl bromides and iodides being more readily and selectively reduced over the corresponding aryl chlorides (Chart 19).

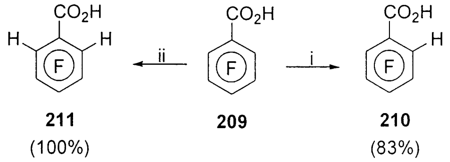
Chart 19. Dechlorination of Organic Chlorides Catalyzed by Low-Valent Nickel Complexes Using $(Ph_3P)_2NiCl_2$ (7.5%), Ph_3P (3%), $Me_2NH\cdot BH_3$ (1.2 equiv), and K_2CO_3 (or Cs_2CO_3) in CH_3CN at 25–50 °C for 6–48 h (84–100%)



Soluble homogeneous organophosphorus–nickel complexes were also used to detoxify PCBs by catalyzed dechlorination using alkoxyborohydride $NaBH_2(OCH_2CH_2OMe)_2$ as the hydrogen source.[258] For instance, decachlorobiphenyl, Arochlor 1221, Arochlor 1232, Arochlor 1254, 2-chlorobiphenyl, and 2,6-dichlorobiphenyl were dechlorinated using $(Et_3P)_2NiCl_2$ and $NaBH_2(OCH_2CH_2OMe)_2$ in THF at 68 °C, in most cases with complete chlorine displacement. The magnitude and position of chlorine displacement were found to be dependent on the cone angle of the organophosphorus ligand. Evidence of the participation of organonickel intermediates was obtained, the isolation of square-planar complexes *p*-$C_6Cl_5C_6Cl_4Ni(Et_3P)_2Cl$, from the reaction of decachlorobiphenyl with $NaBH_2(OCH_2CH_2OMe)_2-(Et_3P)_2NiCl_2$ as the catalyst precursor, and *m*-$C_6Cl_5C_6Cl_4Ni(Et_3P)_2Cl$, from decachlorobiphenyl–$Ni(COD)_2-Et_3P$, at room temperature being of particular interest. Therefore, reactions were proposed to proceed by nickel complex oxidative addition into the carbon–chlorine bond, followed by hydrogenolysis of the metal–carbon bond.

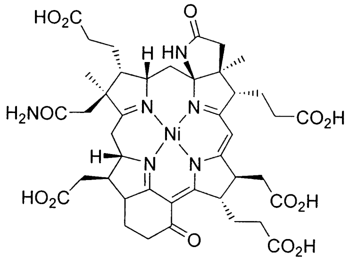
Regioselective *ortho*-hydrodefluorination of pentafluorobenzoic acid (**209**) was achieved by low-valent nickel complexes in situ generated from zinc and $NiCl_2$–2,2′-bipyridine (or 1,10-phenanthroline) complexes.[259] Under these reducing conditions, 2,3,4,5-tretrafluorobenzoic (**210**) and 3,4,5-trifluorobenzoic (**211**) acids were prepared in high yields by using 1 and 5 mol % catalyst, respectively (Scheme 76).

Scheme 76[a]



[a] Reagents and conditions: i, $NiCl_2$, 2,2′-bipyridine (or 1,10-phenanthroline) (1 mol %), Zn, DMF, H_2O (or NH_4Cl); ii, same conditions but 5 mol % catalyst.

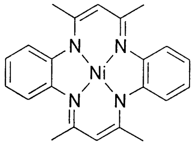
The behavior of coenzyme F_{430} (**212**) was also covered in the study carried out by Wackett et al. on the reductive dechlorination of polychlorinated ethylenes and benzenes catalyzed by transition-metal



212

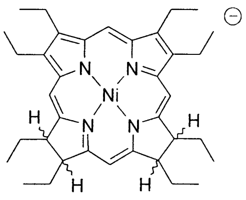
coenzymes, using titanium(III) citrate or dithiothreitol as reductant (see iron and cobalt).[205] As observed for vitamin B_{12}, the order of reductive dechlorination rates for coenzyme F_{430} was carbon tetrachloride > hexachlorobenzene > tetrachloroethylene. Coenzyme F_{430} was capable of sequential dechlorination of tetrachloroethylene to ethylene, also catalyzing the reductive dechlorination of hexachlorobenzene to pentachlorobenzene, though with significantly slower kinetics compared to vitamin B_{12} and hematin.

Taking into account that the framework flexibility of the highly hydrogenated porphyrin in coenzyme F_{430} (**212**) is considered essential in the reduction of Ni(II) to Ni(I), which is the key step in catalysis, a series of nickel(II) complexes with flexible ligands have been developed and applied to the reduction of alkyl halides, thus acting as factor F_{430} mimics. Such is the case for the complex NiL (**213**), where L is the dianion of 6,8,15,17-tetramethyl-5,14-dihydrodibenzo[*b*,*i*][1,4,8,11]tetraazacyclotetradecine, which Sakaki et al. reported to catalyze the reduction of 1-bromoadamantane and chloro-, bromo-, and iodocyclohexane by sodium borohydride in diglyme–ethanol at 30 °C.[260] Due to the electron-donating character of the methoxy groups, the NiL–$NaBH(OMe)_3$ system in diglyme was the most efficient catalytic system examined. A nucleophilic substitution of halide by hydride was initially proposed as a plausible mechanism and was consistent with the observed order of reactivity: bromocyclohexane > 1-bromoadamantane and iodocyclohexane > bromocyclohexane > chlorocyclohexane. However, experiments gave evidence that an electron transfer from the reduced catalyst also has to be considered.



213

The sodium salt of the anion nickel(I) octaethylisobacteriochlorin ($Ni^{I}OeiBC^{-}$) (**214**) was studied as a model of reduced factor F_{430}, reacting extremely rapidly with aliphatic halides in homogeneous DMF solution.[261] The reactivity sequence, methyl > primary > secondary ≥ tertiary, and the rate law were in agreement with an S_N2-like process for the carbon–halogen bond scission. However, the main products of the reactions were derived from free radicals. A wide range of organic halides were tested, hydrogenolysis, coupling, and elimination processes being the general reactions observed for monohalides. With vicinal dihalides, generation of the olefin occurred rapidly, whereas with polyhalomethanes a sequential reductive hydrogenolysis took place. For the methyl and *n*-butyl series, the amount of coupling relative to hydrogenolysis (24–74%) increased mildly in the order Cl < Br < I, whereas the isopropyl halides all showed the same distribution of products, hydrogenolysis occurring to about twice (70%) the extent of coupling.



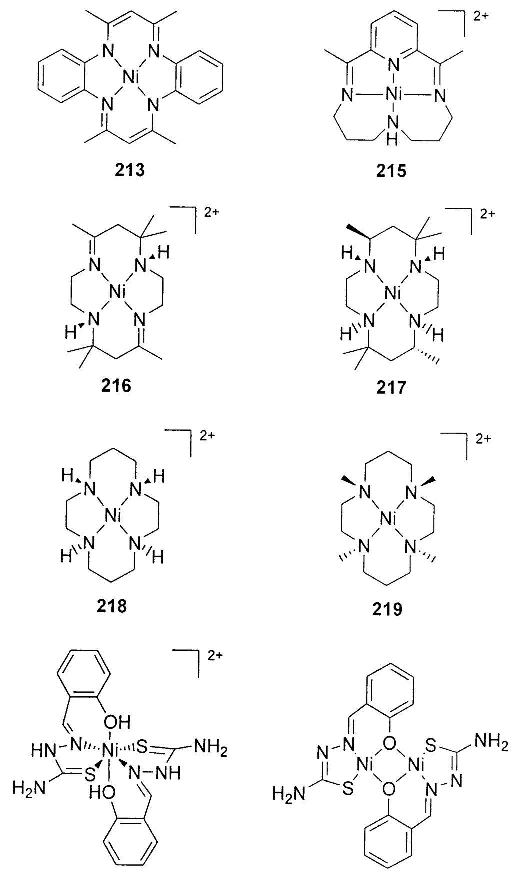
214

The reaction of $Ni^{I}OeiBC^{-}$ (**214**) [generated from Ni^{II}(OEiBC) with sodium amalgam] with alkyl halides was investigated by Stolzenberg et al. in a wide range of solvents,[262a,b] the following observations being noteworthy: (a) the reactions followed a mixed second-order rate law; (b) the reactivity order followed the trend RI > RBr > RCl and MeBr ≫ $Bu^{n}Br$ > $Bu^{s}Br$ > $Bu^{t}Br$; (c) alkyl halides afforded both reduction and coupling products, possessing β-hydrogens also undergoing elimination to give alkenes; (d) polar solvents favored both coupling and alkene formation; (e) in the reduction of methyl halides the hydrogen came from the solvent or residual water in the solvent; (f) the recovery of Ni^{II}(OEiBC) was quantitative even after multiple turnovers; (g) simultaneous addition of the alkyl halide and a proton donor increased the yield of reduction products relative to coupling products.

This research group also reported the ability of coordination nickel complexes **213** and **215**–**221** (Chart 20) to mediate the homogeneous reductive dehalogenation of cyclohexyl bromide by sodium borohydride in various mixed solvents..[262c] Compound **215** was observed to be by far the most effective catalyst, reduction of cyclohexyl bromide being nearly complete in less than 45 min in diglyme–ethanol. The tetracyclam complex **219** was roughly 10 times less active in DMF–ethanol than the unsubstituted cyclam **218**, whereas **220** and **221** exhibited similarities in reactivity in several mixed solvents. The differences between the rate profiles for $NiCl_2{\cdot}6H_2O$ and $Ni(acac)_2$, which form nickel boride in the presence of sodium borohydride, and compounds **213** and **215**–**221** were evidence against a significant role of nickel boride in the reactions catalyzed by the latter. Many mechanisms were suggested that could operate in these processes, involving electron transfer (to afford an alkyl radical), nucleophilic displacement of the halide[262a,b] (to afford an alkyl nickel complex), or formation of nickel hydride or nickel borohydride complexes (serving as hydride-transfer agents in the nucleophilic displacement of the halide).

Nickel(II) complexes **215** and **222** are soluble catalysts able to effect the reductive dehalogenation of aromatic bromides and polychlorobenzenes by sodium borohydride at 25–45 °C in aqueous ethanol, aqueous acetonitrile, or ethanol–acetonitrile.[263] Both

Chart 20

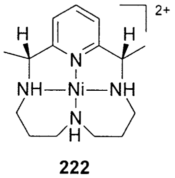


213 215 216 217 218 219 220 221

215 and **222** smoothly reduced structurally different bromoarenes (benzene, naphthalene, and biphenyl derivatives) in good yields (>90%). 1-Chloronaphthalene and chlorobenzene reacted slowly, whereas polychlorobenzenes readily suffered stepwise replacement of chlorine, ester and nitrile functionalities not interfering in any case under these reaction conditions. Deuterium incorporation experiments and rate retardation by adding cumene pointed to a radical-chain mechanism. As an alternative, hydrazine could be used as reductant instead of sodium borohydride.

Nickel−humic acid complexes were found to be good electron-transfer mediators in the reductive dechlorination of TCE using titanium citrate as the bulk reductant. A rapid reaction took place, complete TCE removal being observed after 23 h. Ethane and ethylene were the primary end products, though other nonchlorinated hydrocarbons consisting of methane and C_3−C_6 alkanes were also detected.[264]

Regarding heterogeneous catalysis mediated by nickel, a porous nickel heated in air at 800−1200 °C for 0.25−10 h, followed by activation with hydrogen at 200−600 °C, proved to be a useful catalyst for converting halohydrocarbons such as chlorobenzene and 1,2-dichloropropane into the corresponding hydrocarbons benzene and propane, respectively.[265]



222

One of the most common and accessible reducing agents based on metallic nickel is the so-called Raney nickel,[266] which has been applied by different groups for hydrodehalogenation reactions. For instance, an effective reduction of 1,1-dichlorocyclopropanes to monochlorocyclopropanes was achieved with the system hydrazine−Raney nickel−sodium borohydride.[267]

A series of aryl halides were catalytically hydrodehalogenated by bubbling hydrogen at atmospheric pressure into a biphasic system composed of an organic solvent and an aqueous solution (KOH 50%), in the presence of Raney nickel and a quaternary onium salt as phase-transfer catalyst.[268] The reaction proceeded quickly at mild temperatures (20−50 °C), even for sterically hindered substrates, to afford the corresponding nonhalogenated hydrocarbons in almost quantitative yields. The addition of the quaternary onium salt to the multiphase system induced remarkable effects both in the enhancement of the reduction rate and in the regio- and chemoselectivity of the reaction. For instance, Aliquat 336 allowed the isomeric chloroethylbenzenes to react 50 times faster, *p*-dichlorobenzene was reduced slower than the *ortho*-isomer, and aromatic derivatives were effectively dehalogenated without affecting the carbonyl group present in the molecule.

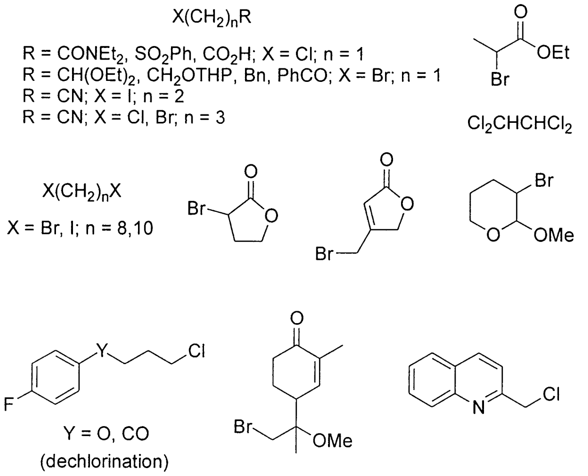
Raney nickel under a pressure of hydrogen and in an aqueous sodium hydroxide solution was utilized for the selective hydrodechlorination of fluorochlorinated substrates such as dichlorofluoroacetic acid, giving rise to fluoroacetic acid in 99% yield.[269]

Ordóñez et al. described the use of Raney nickel catalysts (and supported catalysts) for the hydrodechlorination of organochlorinated aliphatic compounds in discontinuous microreactors at 300 °C and 50 bar. A significant activity was observed toward CCl_4 hydrodechlorination.[270]

The strong reducing ability of the Raney Ni−Al alloy was demonstrated in the quantitative dechlorination of monochlorinated biphenyls in dilute aqueous alkaline solutions, without using any organic solvent, to furnish biphenyl and/or phenylcyclohexane.[271] A higher reducing power was reached when the alkaline solution was dropped slowly into the substrate, when a dilute aqueous KOH or CsOH solution (0.5−1.0%) was used, or when the temperature and the amount of the Raney Ni−Al alloy were increased, thus favoring the formation of phenylcyclohexane (89−91%). Otherwise, as well as using other alkaline solutions, biphenyl was the major reaction product.

Barrero et al. recently reported that Raney nickel was a very efficient reagent for the highly chemoselective reductive dehalogenation of organic halides (Chart 21).[272] Reactions proceeded at room temperature or under refluxing THF with most yields >90%. α-Halocarbonyl compounds and benzyl and allyl halides were easily reduced at room temperature for 5 min to 2 h. Alkyl halides exhibited lower reactivity, alkyl chlorides requiring an excess of Raney nickel under reflux. Therefore, the order of reactivity observed was benzyl = allyl = α-halocarbonyl > alkyl

Chart 21. Organic Halides Reduced with Raney Nickel in THF at rt (or Reflux) for 5 min to 15 h (30−100%)

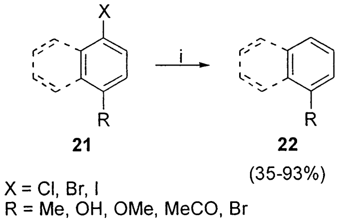


iodide > alkyl bromide > alkyl chloride, no reaction being observed for fluorides and vinyl halides.

Chlorobenzenes were hydrodechlorinated to give benzene in the presence of Zn powder, water, NaOH, and a catalytic amount of metallic Ni in ethanol under a nitrogen atmosphere.[273] The reactions were performed in closed vessels, being accelerated by the addition of an excess of Zn powder, water, and a stoichiometric amount of NaOH to the catalytic system. In this case, water was the hydrogen source, whereas NaOH was the trapping agent of the hydrochloric acid generated.

Active metallic nickel has been prepared by reduction of a nickel salt with a metal and utilized in the hydrodehalogenation of different organic halides. For instance, the metallic-nickel-catalyzed reduction of aryl halides **21** with zinc powder and ethanol was studied by Sakai et al. (Scheme 77).[274] This activated nickel, generated from nickel bromide and zinc, was reported to be colloidal, no reaction taking place in its absence, and the reaction being accelerated by adding an excess of zinc powder to the catalytic system. No coupling products were detected except for benzyl halides. A reaction pathway was proposed for this process in which ethanol was considered the hydrogen source and involving the oxidative adduct ArNiX. The similar reducing system $NiCl_2$−Zn also allowed the conversion of perfluoroalkyl chlorides, such as $Cl(CF_2)_4Cl$, into the corresponding hydroperfluoroalkanes, $H(CF)_2H$, a single-electron-transfer mechanism being proposed for the process.[275]

Scheme 77[a]



[a] Reagents and conditions: i, $NiBr_2$ (3 mol %), Zn, EtOH (or H_2O), 60 °C, 0.5−48 h.

The combination composed of nickel(II) chloride dihydrate, an excess of lithium powder, and a catalytic amount of DTBB (as electron carrier) was successfully applied by Yus et al. to the hydrodehalogenation of different organic chlorides, bromides, and iodides **74**, at room temperature (Scheme 78).[276a] This system found application for alkyl and aryl halides, though fluorides remained unaltered. As an example, 3,5-dichlorophenol was transformed into phenol in 90% isolated yield. One main advantage of this methodology is the use of the corresponding deuterated nickel salt, giving rise to a series of deuterated hydrocarbons **75**. It was suggested that very finely and reactive metallic nickel was obtained at the same time that molecular hydrogen (or deuterium) was in situ generated, which adsorbed on the surface of the metal would induce the dehalogenation process. Alternatively, a catalytic hydrodehalogenation was performed with external molecular hydrogen and catalytic nickel(0), prepared from anhydrous nickel(II) chloride, lithium, and a catalytic amount of naphthalene.[276b]

Scheme 78[a]

$$\underset{\mathbf{74}}{RX} \xrightarrow{i} \underset{\mathbf{75}}{RH(D)}$$

(80-99%)

R = $CH_3(CH_2)_9$, $HO(CH_2)_6$, $Ph(CH_2)_2$, Ph_3C, p-$HOCH_2C_6H_4$, p-HOC_6H_4, p-$H_2NC_6H_4$; X = Cl
R = $CH_3(CH_2)_{15}$, $HO(CH_2)_6$, p-MeC_6H_4, p-PhC_6H_4; X = Br
R = $Ph(CH_2)_2$; X = I

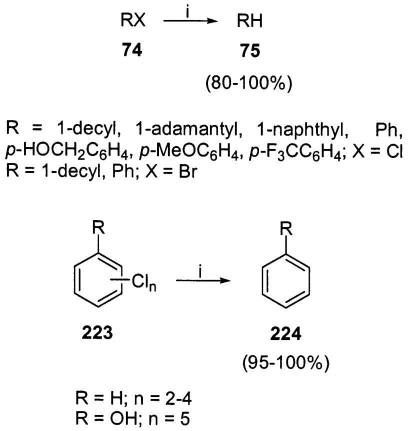
[a] Reagents and conditions: i, $NiCl_2{\cdot}2H_2O$ (or $NiCl_2{\cdot}2D_2O$), Li, DTBB (5 mol %), THF, rt, <4 h.

Nickel-containing complex reducing agents (NiCRA) were discovered by Caubère et al.[277] A mixture of lithium hydride, *tert*-butyl alcohol, and nickel acetate heated at 63 °C in THF (or DME) led to a new nickel-containing complex reducing agent called LiH−NiCRA.[278] Aromatic (1-bromonaphthalene, 1-bromo-2-methylnaphthalene, and 1-chloronaphthalene) and primary alkyl bromides and chlorides (1-chloro and 1-bromododecane) were quantitatively reduced by this reagent in 3−6 h in DME. Tertiary bromide 1-bromoadamantane was reduced at almost the same rate as the primary halides, whereas 1-chloroadamantane was slowly reduced, yielding 37% adamantane after 24 h. LiH−NiCRA exhibited attenuated reducing properties in comparison with NaH−NiCRA.

Powder alkali-metal hydrides (MH, M = Li, Na, K) of nanometric size, in the presence of catalytic amounts of nickel(II) acetate, were shown to be more efficient than the alkali-metal hydrides alone in the reduction of organic halides.[279] Both alkyl and aryl halides, including fluorides, were hydrodehalogenated, cobalt(II) chloride and titanium tetrachloride being alternative promoters to nickel(II) acetate. A remarkable synergistic effect was observed when the combination $Ni(OAc)_2$−$TiCl_4$−$NaOPr^i$ was used as catalyst, allowing the quantitative reduction of chloro-, bromo-, and fluorobenzene in 2 h, and that of fluorotoluenes in 3−4 h in THF at 66 °C.

Fort et al. prepared subnanometrical nickel−aluminum clusters by reduction of equimolar amounts of nickel(II) acetate and aluminum acetylacetonate, induced by alkoxide-activated sodium hydride.[280a] These bimetallic clusters exhibited a high catalytic activity for the efficient reductive dehalogenation of aliphatic and aromatic halides **74**, as well as polychlorinated arenes **223** (Scheme 79).[280b] In aromatic halides, the presence of electron-donating groups decreased the reduction rate, whereas electron-withdrawing groups had a weak effect. The dechlorination of polychlorobenzenes or 4,4′-dichlorobiphenyl led to benzene and biphenyl as the sole reaction products, respectively. A mechanism with participation of nickel hydride species, from the adsorption of molecular hydrogen on the surface of the Ni−Al catalyst, was proposed. The synergistic effect of these bimetallic Ni−Al clusters on the catalytic activity compared to Ni clusters[280c,d] was attributed to the increased dispersion of nickel species in the subnanometric aluminum matrix.

Scheme 79[a]



R = 1-decyl, 1-adamantyl, 1-naphthyl, Ph, p-HOCH$_2$C$_6$H$_4$, p-MeOC$_6$H$_4$, p-F$_3$CC$_6$H$_4$; X = Cl
R = 1-decyl, Ph; X = Br

R = H; n = 2-4
R = OH; n = 5
R = p-ClC$_6$H$_5$; n = 1

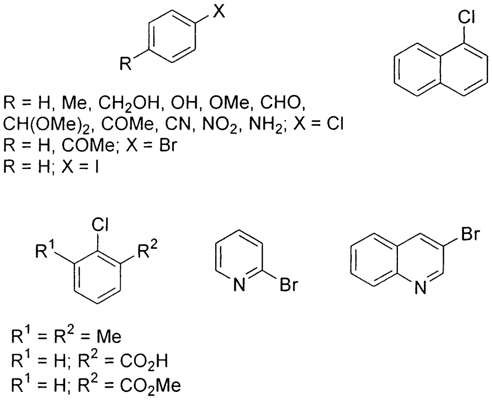
[a] Reagents and conditions: i, Ni−Al cluster (10 mol%), THF, reflux, 0.25−110 h.

One of the most successful combinations used as reducing agents is that composed of a borohydride and a nickel salt. More specifically, it is known that nickel chloride solutions can be reduced by sodium borohydride to give a black colloidal material named “nickel boride”, which possesses a reactive form of hydrogen on the surface of the solid capable of causing both hydrogenation and hydrogenolysis reactions, among other processes.[281]

In this context, Pittman et al. carried out a comparative study on the dechlorination of aromatic chlorides by different reducing systems including TEG−KOH, $NaBH_4$−THF, $NaBH(OMe)_3$−THF, and $NaBH_2(OCH_2CH_2OMe)_2$−THF. However, the best results were obtained by portionwise addition of nickel chloride to the alkoxyborohydride $NaBH_2(OCH_2CH_2OMe)_2$ in THF at 68 °C. Under these conditions very high or complete dechlorination of the PCB Arochlor 1016, chloro-p-xylene, α-chlorotoluene, 4-chlorobiphenyl, pentachlorophenol, and 1,2,4-trichlorobenzene was achieved.[282]

The borohydride exchange resin (BER)−nickel(II) acetate system proved to be capable of reducing aryl halides in methanol, at room temperature or under reflux for 1−3 h, and in excellent yield and selectivity (Chart 22).[283a,b] Although this system did not reduce fluorobenzene, it tolerated hydroxymethyl, phenol, methoxy, acetal, carboxy, ester, cyano, and amino functionalities. Overreduction of 1-chloronaphthalene and 3-bromoquinoline to the corresponding tetrahydro derivatives, along with the expected products, was also observed. This methodology was extended to primary, secondary, and tertiary alkyl open-chain and cyclic alkyl bromides and iodides, as well as to benzylic chlorides and iodides, α-haloesters, and amides, all of which were quantitatively reduced in 3 h.[283c]

Chart 22. Organic Halides Dehalogenated with BER−Ni(OAc)$_2$ in MeOH at rt (or Reflux) for 1−3 h (81−99%)



R = H, Me, CH$_2$OH, OH, OMe, CHO, CH(OMe)$_2$, COMe, CN, NO$_2$, NH$_2$; X = Cl
R = H, COMe; X = Br
R = H; X = I

R^1 = R^2 = Me
R^1 = H; R^2 = CO$_2$H
R^1 = H; R^2 = CO$_2$Me

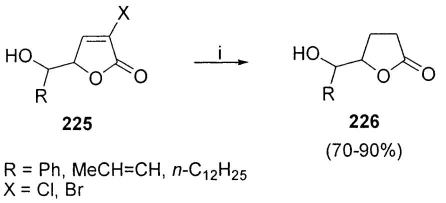
A series of PCB congeners (monochloro-, dichloro-, and trichlorobiphenyls) were hydrodechlorinated by sodium borohydride and homogeneous or heterogeneous nickel catalysts.[284] In the absence of nickel compounds, very little reaction occurred, but in the presence of solid nickel boride or soluble tetrakis(triphenylphosphine)nickel(0) complex, extensive hydrogenolysis took place at ambient temperature in DMF. The most interesting result from the nickel boride hydrogenolysis was that the more hindered 2-chlorine atoms were removed at a rate comparable to those at the 3- and 4-positions. On the other hand, with the nickel(0) complex the preferred position of hydrogenolysis was either the 3- or the 4-position. This selectivity was interpreted considering the known mechanism of oxidative addition of aryl halides with nickel(0) complexes.

A nickel boride, prepared in situ by the reaction of nickel chloride with sodium borohydride, was also used for the hydrodechlorination of PCBs (Arochlor 1248), polychlorinated naphthalenes (PCNs), chlorobenzene, and tetrachloroethylene.[285] Reactions were carried out in 2-propanol at room temperature, the reaction being alternatively sustained (once initiated) by bubbling hydrogen gas into the reaction mixture. In general, reactions were fast (20−70 min) and led to biphenyl (and dicyclohexyl), naphthalene, benzene, and ethylene, respectively, with moderate to good yields (70−89%). However, saturated species such as dichloromethane and polychlorinated alkanes (C_{14}−C_{17}) did not react.

The in situ reaction of sodium borohydride with 2-methoxyethanol in 2-propanol, in the presence of a catalytic amount of nickel(II) chloride hexahydrate, generated a powerful dechlorinating agent able to dechlorinate DDT to 1,1-diphenylmethoxymethane (80%) and 1-(4-chlorophenyl)-1-phenylethane (10%) in 6 h at 82−84 °C.[286] The method was shown to be very sensitive to reagent ratios, resulting in a lower percentage of dechlorination when either the nickel salt or 2-methoxyethanol was not present in the reaction mixture. LAH in the presence of catalytic amounts of nickel(II) chloride reduced various triarylvinyl halides **191** to the corresponding alkenes **192** (see Scheme 68 and the corresponding comments).[207]

More recently, a series of 2,5-dihydrofuran-2-ones **225**, halogenated at the 3-position, were reported to undergo both carbon−carbon double bond reduction and hydrodehalogenation with $NiCl_2$ and $NaBH_4$ in THF−MeOH to furnish the desired γ-butyrolactones **226** (Scheme 80).[287]

Scheme 80[a]



[a] Reagents and conditions: i, $NiCl_2$, $NaBH_4$, THF, MeOH, 0 °C, 10 min.

The vapor-phase hydrodechlorination of CCl_2-$FCClF_2$ was promoted by the mixed oxide NiO−Cr_2O_3 at around 400 °C, especially by a mixture containing 70% Cr.[288] The catalytic activity of the system was well maintained with time, no promotion being observed with Cr_2O_3 alone. Methane formation and catalyst deactivation due to a carbonaceous deposit on the surface were observed with NiO or NiO−Cr_2O_3 containing smaller amounts of Cr_2O_3. The excellent behavior of NiO−Cr_2O_3 with 70% Cr content was attributed to $NiCr_2O_4$ being dispersed by Cr_2O_3 on the surface.

Several Ni−Mg−Al and Ni−Al hydrotalcite-like precursors were prepared to study their catalytic properties in the gas-phase hydrodechlorination of 1,2,4-trichlorobenzene. It was observed that increasing the magnesium content in the catalyst greatly increased both the activity and selectivity to benzene at the time that the deactivation of the catalyst became slower.[289]

Detoxification methodologies have been settled on the basis of the use of nickel-supported catalysts as effective dehalogenation agents. For instance, Ni/TiO_2 catalysts (prepared by treating Ti−Ni−H_n hydrides with concentrated hydrochloric acid) were utilized for the hydrodechlorination of 1,1,2-trichloro-1,2,2-trifluoroethane (Freon R-113) into chlorofluoroethylene.[290]

Hydrodechlorination of *o*-dichlorobenzene was studied in the gas phase at 300 °C and 2 MPa over reduced and sulfided Ni, Mo, and Ni−Mo catalysts supported on alumina.[291] The work was related to disposal of chlorinated organic wastes containing sulfur impurities. Positive synergism in activity between Ni and Mo was observed with sulfided Ni−Mo catalyst, the Ni−Mo sample being 3 times more active than the sum of the activities of Ni and Mo samples. Chlorobenzene was observed as an intermediate over all catalysts. The catalyst Ni−Mo/γ-Al_2O_3 also found application in the hydrodechlorination of hexachlorobenzene (325 °C),[292a] 1,2-dichlorobenzene,[292b] chloropyridols (275−325 °C),[292c] 1,2,3-trichlorobenzene (200−350 °C),[293a−c] chlorobenzene (300−340 °C),[293d,e] PCBs (250−350 °C),[293f−i] polychlorinated ethanes and ethenes,[294] and chloroethyl ethyl sulfide.[295] A comparative study on the hydrodehalogenation activity and selectivity of Ni−Mo/ γ-Al_2O_3 with carbon-supported sulfides of various transition-metal elements was also reported.[296]

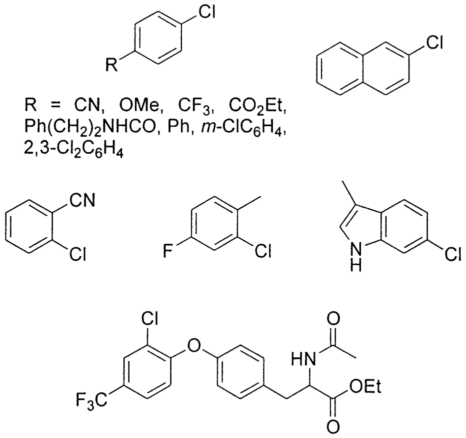
Heterogeneous nickel-containing catalysts based on graphite oxide were prepared and their activities tested in the dechlorination of polychlorinated aromatic hydrocarbons by different high-boiling-point organosilanes such as $Et(Bu^tO)_2SiH$.[297] Oxidation of the catalyst precluded it from being reused.

Sueiras et al. studied the conversion of CFC-12 and HCFC-22 with hydrogen between 250 and 290 °C at atmospheric pressure over nickel, graphite-supported nickel, activated carbon-supported nickel, nickel−potassium oxide, nickel−copper, and nickel−aluminum oxide catalysts.[298a] The most common reactions are those which allow the removal of one chlorine atom during one sojourn on the surface of the catalyst, and then removal of two new halogen atoms, a consecutive mechanism being proposed. Coupling products such as C_2H_6, C_2F_4, $C_2H_2F_4$, $C_2H_4F_2$, and $C_2Cl_2F_4$ were also obtained. Hydrodechlorination of 1,2,4-trichlorobenzene on several Ni/Al_2O_3 and $Ni/NiAl_2O_4$ catalysts was also studied, the extent of the reaction being related to the amount of hydrogen available at the reaction temperature, the most selective catalysts to benzene being those which had the highest amounts of hydrogen desorbing at lower temperatures.[298b,c] Fresh and reactivated $Ni/NiAl_2O_4$ hydrogenated 1,2,4-trichlorobenzene to cyclohexane in 30 min at 250 °C, an irreversible partial chlorination of the catalytic surface making the hydrogenation of the aromatic ring difficult.[298d,e] An electrophilic-type reaction was suggested for the gas-phase hydrodechlorination of substituted chlorobenzenes on Ni/γ-Al_2O_3.[299]

Lipshutz et al. developed a new method for the reduction of aryl chlorides to the corresponding arenes mediated by the heterogeneous catalyst nickel on charcoal.[300] Thus, treatment of an aryl chloride with dimethylamine−borane complex and potassium carbonate, under the influence of 5% nickel on charcoal and 20% triphenylphosphine in refluxing acetonitrile, required only 5−10 h to effect complete reduction (Chart 23). Substrates bearing *ortho*-substituents were smoothly reduced, while both electron-rich and electron-poor groups afforded similar results at similar rates. This method was compatible with the presence of cyano, ester, amide, or ether functionalities but not with aldehyde or ketone moieties, mono-, di-, and trichlorobiphenyls being successfully converted to biphenyl.

A series of Ni/C composite catalysts were prepared by a modified carbothermal reduction method involving the use of ion-exchange resins. The catalyst

Chart 23. Aryl Chlorides Dehalogenated with 5% Ni/C, 20% Ph_3P, $Me_2NH{\cdot}BH_3$, and K_2CO_3 in 2% aq MeCN at Reflux for 5−10 h (91−100%)


R = CN, OMe, CF_3, CO_2Et, $Ph(CH_2)_2NHCO$, Ph, *m*-ClC_6H_4, 2,3-$Cl_2C_6H_4$

activities and selectivities were studied in the hydrodechlorination of chlorobenzene to benzene, a dependence on the carbothermal reduction temperature during their preparation being observed. In general, the catalysts exhibited good stabilities and selectivities, even in the presence of the hydrogen chloride produced during the reaction.[301]

The catalytic hydrodehalogenation of aromatic halides has been recently effected on silica-supported nickel catalysts by Keane et al.[302] Reactions were carried out in the gas phase at temperatures ranging from 200 to 300 °C with Ni/SiO_2 (1.5−20.3%) and applied to the following starting materials: chlorobenzene, chlorotoluene, chlorophenol, dichlorobenzene, dichlorophenol, trichlorophenol, pentachlorophenol, and bromobenzene. Hydrodehalogenation was proposed to occur via an electrophilic mechanism where the presence of electron-donating substituents on the benzene ring enhanced the rate of the reaction. Polychlorinated materials were stepwise dechlorinated, generating partially dechlorinated products. Hydrodechlorination yields and rates of the parent aromatic from the polychlorinated substrate were shown to be favored by larger nickel particle sizes.

Reductive dechlorination of 1,2-dichloroethylene to ethylene was accomplished by molecular hydrogen or ammonia with nickel [from nickel(II) nitrate] supported on porous clay at 250−500 °C.[303] On the other hand, nickel supported on zeolites (NiZSM-5) found application in the catalytic hydrodehalogenation of bromotrifluoromethane (Halon 1301) with methane between 300 and 500 °C at ambient pressure.[304] It was found that the incorporation of nickel into the zeolite HZSM-5 significantly enhanced its activity. A variety of products were formed during the reaction including CH_3Br, CHF_3, CH_2Br_2, C_2F_6, C_2H_4, C_2H_2, $C_2H_2F_2$, $CHBrF_2$, CH_2BrF, and C_2H_3Br. Deactivation of the catalyst was due in part to poisoning by halogens. NiZSM-5 in combination with hydrogen also allowed the complete hydrodehalogenation of different halogenated aliphatic hydrocarbons.[305] By using an expanded clay aggregate, CaHY zeolite, and high-silica zeolite as carriers of nickel-containing catalysts, hydrodechlorination of 1,2,4-trichlorobenzene led to a mixture of monochlorobenzene, dichlorobenzenes, and benzene.[306]

F. Group VIIIB. Second Triad: Ru, Rh, Pd

1. Ruthenium

A large variety of ruthenium complexes have been prepared hitherto, many of them showing remarkable catalytic activities and therefore having a great potential for the discovery of novel catalytic reactions and development of new synthetic methods.[307] As described below, some of these catalysts found application in hydrodehalogenation reactions under homogeneous or heterogeneous conditions.

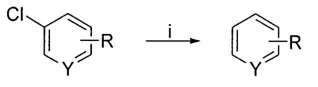
The complex $RuCl_2(Ph_3P)_3$ acted as a catalyst in the hydrogenolysis of carbon tetrachloride and trichlorofluoromethane ($CFCl_3$) into chloroform and dichlorofluoromethane ($CHFCl_2$), respectively, under mild reaction conditions (25 °C, 810 Torr, mixed solvent containing toluene and ethanol or methanol).[308] Reduced reactivity was observed with the chelate complex $RuCl_2(dppe)_2$, but good conversion of carbon tetrachloride into chloroform was also obtained with the hydride complex $RuHCl(Ph_3P)_3$. $CFCl_3$ was transformed into $CHFCl_2$ by $RuCl_2(Ph_3P)_3$ and hydrogen with a catalytic turnover of 17 after 24 h at 25 °C, no chlorofluoromethane being detected. However, this system could not be successfully applied to the hydrogenolysis of dichlorodifluoromethane (CF_2Cl_2) since it only yielded small quantities of CHF_2Cl.

Highly selective hydrogenolysis of CFC-113a (CF_3CCl_3) to produce HCFC-123 (CF_3CHCl_2) was achieved under 8 atm of molecular hydrogen in THF at 100 °C for 5 h, in the presence of any of the ruthenium catalysts $RuCl_2(Ph_3P)_3$, $RuH(NO)(Ph_3P)_3$, RuH(NO)(etp) [etp = bis(diphenylphosphinoethyl)phenylphosphine], $Ru(NO)_2(Ph_3P)_2$, and $RuCl(NO)(Ph_3P)_2$.[309] The best conversion (>99%) was reached with $RuCl(NO)(Ph_3P)_2$, whereas the complex $Ru(NO)_2(Ph_3P)_2$ showed reduced activity, the addition of a large excess of free phosphines making the catalytic system more efficient. An oxidative addition of the carbon−chlorine bond via an S_N2 mechanism or an electron-transfer mechanism was suggested.

Bényei et al. reported the catalytic transfer hydrodehalogenation of carbon tetrachloride, chloroform, and 1-hexyl halides catalyzed by water-soluble ruthenium(II) phosphine complexes.[310] Thus, carbon tetrachloride was transformed into chloroform and dichloromethane using an aqueous solution of sodium formate as hydrogen donor and the complex $RuCl_2(TPPMS)_2$ (TPPMS = *m*-sulfophenyldiphenylphosphine sodium salt). Under these conditions, a very high turnover frequency was obtained for carbon tetrachloride, the yield of chloroform being more than 50% in 3 h, but no dehalogenation was observed for chlorobenzene. Benzyl chloride was cleanly transformed into toluene with the above catalyst, whereas for 1-hexyl halides (X = Cl, Br, I) the complex $Ru(H_2O)_3(PTA)_3(Ts)_2$ (PTA = 1,3,5-triaza-7-phosphaadamantane) was the catalyst of choice.

Grubbs et al. proved that the complexes $RuH_2(H_2)_2(PCy_3)_2$ and $RuHCl(H_2)_2(PCy_3)_2$ were excellent catalysts for the dechlorination of aryl chlorides **227** (Scheme 81).[311] Reactions were performed in secondary alcohols, in the absence of dihydrogen, and were complete in 1 h. The catalysts were tolerant to a

Scheme 81[a]



227 **228**

(100% conversion)

Y = CH; R = H, *o*-Me, *m*-Me, *p*-Me, *p*-MeO, fused benzene, *o*-Cl
Y = N; R = H

[a] Reagents and conditions: i, $RuHCl(H_2)_2(PCy_3)_2$, Bu^sOH, 50% NaOH, 80 °C, 1 h.

variety of functional groups and were also efficient in the dechlorination of polychlorinated arenes. Alternatively, the catalytic species could be generated in situ from the air-stable precursor $[RuCl_2(COD)]_n$, Cy_3P, and molecular hydrogen, the conversions obtained being comparable to those using the isolated catalyst. The experimental results, especially the identification of the ketone generated in the course of the reaction, supported the proposed mechanism involving hydrogen transfer, the secondary alcohols acting as hydrogen sources.

The catalytic activity of the complexes $FeCl_2(Ph_3P)_2$, $RuHCl(Ph_3P)_3$, $RuH_2(CO)(Ph_3P)_3$, $RuHCl(CO)(Ph_3As)_3$, $RuHCl(CO)(Pr^i{}_3P)_2$, $OsHCl(CO)(Pr^i{}_3P)_2$, $OsH_2Cl_2(Pr^i{}_3P)_2$, $CoCl(Ph_3P)_3$, $RhH_2Cl(Pr^i{}_3P)_2$, $IrH_2Cl(Pr^i{}_3P)_2$, $IrCl(Ph_3P)_3$, and $IrH_2(SiEt_3)(COD)(Cy_3P)$ was studied in the simultaneous dehalogenation of 1,2,4-trichlorobenzene and the chlorination of triethylsilane.[312] The 3d-metal complexes and the derivative $IrH_2(SiEt_3)(COD)(Cy_3P)$ were shown to be inactive, whereas the 4d- and 5d-metal compounds simultaneously catalyzed the dehalogenation of 1,2,4-trichlorobenzene and the chlorination of Et_3SiH. The ruthenium and rhodium derivatives were the most effective ones, osmium and iridium derivatives undergoing deactivation. The complexes $RuHCl(Ph_3P)_3$ and $RhH_2Cl(Pr^i{}_3P)_2$ also catalyzed the dehalogenation of chlorobenzene and 1,2- and 1,4-dichlorobenzene, the dehalogenation of 1,4-dichlorobenzene being favored over that of the 1,2-isomer.

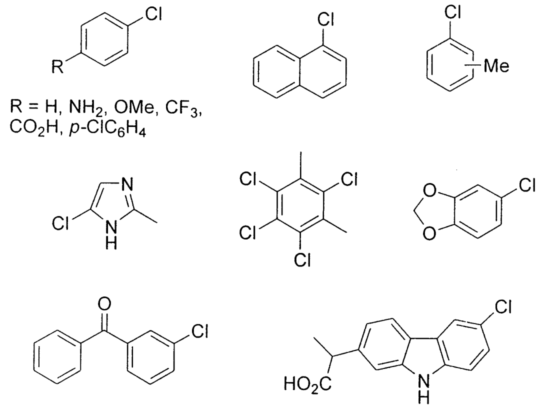
Mono-, bi-, and trinuclear ruthenium complexes with various ligands on the surface of silica gels modified with aminopropyl, formamido, sulfide, cyano, or mercapto groups catalyzed the hydrodehalogenation of *p*-bromotoluene by transfer of hydrogen from sodium borohydride in 2-propanol, both in an argon atmosphere and in air.[313] The immobilized binuclear ruthenium(II,III) tetraacetate exhibited a higher catalytic activity in the hydrogenolysis of *p*-bromotoluene than heterogenized mononuclear systems.

A ruthenium on activated carbon catalyst (Ru/C) was revealed to be convenient for hydrodechlorination and hydroaromatization of 13 different mono-, di-, tri-, tetra-, and pentachlorophenols under mild reaction conditions (25–80 °C, 0.3–0.5 MPa).[314] Sodium hydroxide added to the solution behaved as a cocatalyst, neutralizing hydrochloric acid formed, then preventing poisoning of the metallic surface, neutralizing the acidic sites of the activated carbon, and forming the corresponding phenoxides, which easily suffered desorption from the active carbon, therefore making them more reactive to hydrogenation. A chlorophenol → phenol → cyclohexanol consecutive kinetic scheme was considered. The catalyst was also efficient for *o*-chloroaniline and 4,4′-dichlorobiphenyl. Considerable selectivity toward $CHClF_2$ was observed in the hydrodechlorination of CCl_2CF_2 with a Ru/C catalyst.[315]

2. Rhodium

Rhodium trialkylphosphine complexes have certain properties which make them suitable for a wide range of catalytic reactions, some of which are the only systems available or are the catalysts of choice.[316] Thus, the rhodium(III) complexes $L_2Rh(H)Cl_2$ ($L = Cy_3P$, $Pr^i{}_3P$) were shown by Alper et al. to be excellent catalysts for the hydrogenolysis of chloroarenes under biphasic conditions (40% NaOH, PhMe), or to give somewhat higher product yields under phase-transfer conditions, using benzyltriethylammonium chloride as the quaternary ammonium salt.[317] Many functional groups were compatible with the carbon–chlorine cleavage process (Chart 24).

Chart 24. Hydrodechlorination of Chloroarenes with $[(Cy_3P)_2Rh(H)Cl_2]$ (1–20 mol %), 40% NaOH, PhMe, and $PhCH_2NEt_3Cl$ at 25–100 °C for 3–48 h (45–97% Yield)



A rhodium catalyst prepared by dissolving $(Cp^*RhCl_2)_2$ in 2-propanol in the presence of triethylamine was used in the homogeneous catalytic hydrodehalogenation of chloroaromatics (chlorobenzene, 1,2,3-trichlorobenzene, and 1-chloronaphthalene) under 600 psi of H_2 at 75 °C for 180–360 min.[318] The corresponding aromatic hydrocarbons were obtained as intermediates which suffered in situ hydrogenation to the saturated hydrocarbons (>97% yield).

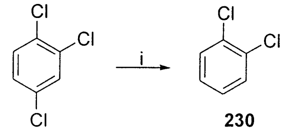
The selective hydrogenolysis of CFC-113a (CF_3CCl_3) to give HCFC-123 (CF_3CHCl_2), previously described with ruthenium complexes, was also achieved under 8 atm of molecular hydrogen in THF at 100 °C for 5 h with the rhodium complexes $RhCl(Ph_3P)_3$, $RhH(Ph_3P)_4$, and $RhCl_3Py_3$, the first one reaching the maximum conversion (98%).[309] In the case of the complex $RhCl(Ph_3P)_3$, the reaction rates were dependent on the concentration of chloride ions added, an S_N2 mechanism for the oxidative addition of CFC-113a being proposed.[319] When the complex $RhCl(Ph_3P)_3$ was applied to the hydrogenolysis of CFC-113 ($CF_2ClCFCl_2$), HCFC-123a ($CF_2ClCHClF$) and chlorotrifluoroethene ($CF_2{=}CFCl$) (product from β-elimination) were obtained. The complex RhCl-

$(Ph_3P)_3$ also found application in the hydrodechlorination of CCl_3CF_3 under hydrogen in benzene to give selectively $CHCl_2CF_3$ in >95% yield (at 45% conversion) after 4.5 h, no CH_2ClCF_3 being detected.[320]

Homogeneous catalysts prepared from rhodium(III) chloride in aqueous aromatic amines reduced carbon–chlorine bonds under mild water gas shift conditions (100 °C, 1 atm of CO).[321] In a 4-picoline–water solvent mixture, 1,2-dichloroethane was hydrodechlorinated to give ethane and ethylene in yields compatible with those of the consumption of the reducing agent CO and formation of CO_2. A moderate dependence of activity on the basicity of the aromatic amine was observed, a methyl group at the α-position exercising a strong negative steric effect.

Esteruelas et al. studied the dehalogenation of polychloroarenes with triethylsilane catalyzed by a new rhodium homogeneous system, obtained by in situ reaction of the dimer $[Rh(\mu\text{-}Cl)(COE)_2]_2$ (COE = cyclooctene) with triphenylphosphine.[322a] This system catalyzed the selective dechlorination of 1,2,4-trichlorobenzene (**229**) to 1,2-dichlorobenzene (**230**) and subsequently the dechlorination of the latter substrate to chlorobenzene and benzene (Scheme 82).

Scheme 82[a]



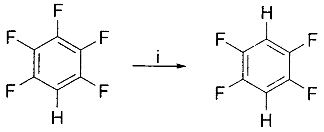
229 **230** (96%)

[a] Reagents and conditions: i, $(Me_3P)_3RhC_6F_5$, H_2 (85 psi) [or $(EtO)_3SiH$], Et_3N, 95–100 °C.

1,3- and 1,4-dichlorobenzene were not observed during the dechlorination of 1,2,4-trichlorobenzene, but both substrates were readily and selectively dehalogenated to chlorobenzene. The best results were obtained for a rhodium complex:triphenylphosphine molar ratio of 1:3, the complex $RhCl(Ph_3P)_3$ also being an effective catalyst for the dehalogenation of 1,2,4-trichlorobenzene. Alternatively, the selective dechlorination of 1,2,4-trichlorobenzene depicted in Scheme 82 was also effected by transfer hydrogenation with sodium formate in 2-propanol catalyzed by $RhCl(Ph_3P)_3$.[322b] Under these conditions, hydrogenolysis of 1,3- and 1,4-dichlorobenzene was found to be sequential to give first chlorobenzene followed by benzene.

As already commented on in this review, much research effort has been devoted to the activation of the strong carbon–fluorine bond.[23] Milstein et al. discovered that catalytic activation of carbon–fluorine bonds could be achieved by the soluble rhodium complexes $(Me_3P)_3RhC_6F_5$ and $(Me_3P)_4RhH$.[323a] Thus, heating hexafluorobenzene or pentafluorobenzene with any of these complexes at 95–100 °C in the presence of a base (triethylamine or a mixture of triethylamine and potassium carbonate) under 85 psi of hydrogen led to fluorine–hydrogen exchange and capture of hydrogen fluoride by the base. The complex $(Me_3P)_3RhC_6F_5$ was more effective than $(Me_3P)_4RhH$, which in turn was more effective than $(Ph_3P)_4RhH$. Hexafluorobenzene was more reactive than pentafluorobenzene (**171**), the latter undergoing regioselective carbon–fluorine activation at the *para*-position and giving rise to 1,2,4,5-tetrafluorobenzene (**231**) (Scheme 83). This behavior was also observed when the reaction was carried out with the complex $(Me_3P)_3RhC_6F_5$ and silane $(EtO)_3SiH$ as hydrogen source instead of molecular hydrogen.[323b] The proposed catalytic cycle for hydrogenolysis involves electron-rich hydridorhodium(I) phosphine complexes as the species that induce cleavage of carbon–fluorine bonds.

Scheme 83[a]



171 **231**

[a] Reagents and conditions: i, $[Rh(\mu\text{-}Cl)(COE)_2]_2$, Et_3SiH, Ph_3P, *p*-xylene, 78 °C, 65 min.

Carbon–fluorine bond activation in different polyfluorinated arenes with the complex $Cp^*Rh(Me_3P)H_2$ was also reported.[324] The complex $(Cy_3P)_2Rh(H)Cl_2$ was used by Grushin et al. for the catalytic activation of the carbon–fluorine bond in 1-fluoronaphthalene.[325] The reaction was carried out in 40% NaOH at 95 °C and 80 psi of hydrogen, furnishing naphthalene in >90% selectivity at 45% conversion after 20 h. Under 135 psi of hydrogen for 48 h, 90% conversion of 1-fluoronaphthalene was obtained. Similar results were obtained for fluorobenzene, *p*-fluorotoluene, *m*-fluoroanisole, and *p*-fluoroaniline.

Supported rhodium catalysts have also been utilized for hydrodehalogenation processes, carbon-supported rhodium catalysts having been extensively studied by Ukisu et al. This group observed that hydrogen-transfer dechlorination of PCBs[326a] (to biphenyl and phenylcyclohexane) and 1,2,4-trichlorobenzene[326b] (to benzene) effectively occurred in a 2-propanol solution of a base such as sodium or potassium hydroxide, in the presence of carbon-supported noble metal catalysts (Rh/C, Pd/C, Ru/C, and Pt/C) at temperatures below 82 °C. Rh/C catalyst proved to be the most active, followed by Pd/C, Pt/C, and Ru/C. In the case of 1,2,4-trichlorobenzene, the reaction time was readily reduced to 0.5 h by increasing the amount of catalyst and elevating the reaction temperature from 65 to 82 °C. A high yield of benzene containing deuterium atoms was obtained when deuterium-labeled 2-propanol was used as solvent, therefore confirming the hydrogen-transfer pathway. This methodology was extended to other aromatic chlorides such as chlorobenzene, *p*-chlorotoluene, and 4-chlorobiphenyl.[326c,d] For these substrates the composite catalysts Rh–Pt/C and Rh–Pt/TiO_2 displayed significant activities at temperatures below 35 °C. It was proposed that the hydrogen species arising from dehydrogenation of 2-propanol on Pt particles controlled the reduced state of Rh, facilitating the generation of active Rh sites, which in turn were responsible for the hydrogen transfer from 2-propanol to the organic chloride.

Hydrodechlorination of 1,2-dichloroethane and TCE was investigated over Rh/ SiO_2 catalysts at 92–280

°C and 0.1 MPa of H_2.[327] Ethane and hydrogen chloride were the major reaction products, the selectivity toward ethane increasing with temperature. Partially dechlorinated compounds such as C_2H_5Cl (from 1,2-dichloroethane) and C_2H_5Cl, $C_2H_4Cl_2$, C_2H_3Cl, and $C_2H_2Cl_2$ (from TCE) constituted the minor products, the selectivity for the partially dechlorinated C_2 hydrocarbons decreasing with increasing temperature. Although chlorine dissociation from chlorinated hydrocarbons poisoned the catalyst, >70% regeneration of the initial activity was achieved by hydrogen treatment.

The structure of rhodium(II) complexes with vigorous ligands inmobilized on γ-aminopropyl-containing silica gel and polymers with 5-methylpyrazole and imidazole groups was investigated.[328] For acetonitrile and hexafluoroacetylacetonate complexes a replacement of the ligands by the amino groups of the carrier was observed. On the other hand, the complex $Rh_2(CH_3CO_2)_4$ was significantly more active than other metal complexes inmobilized on γ-aminopropyl-containing silica gel, in the hydrodehalogenation of *p*-bromotoluene by transfer of hydrogen from sodium borohydride and 2-propanol.

Blum et al. studied the heteronuclear complex $Rh_2Co_2(CO)_{12}$ physically entrapped in SiO_2−sol−gel matrixes, which was utilized as a recyclable catalyst in the hydrogenolysis of 1-chloronaphthalene (3.4 atm of H_2, 30 °C, 22 h) to give mainly the overreduced products *cis*- and *trans*-decalin (82% and 12%, respectively).[253b] The SiO_2−sol−gel-entrapped ion pair $[(C_8H_{17})_3NMe]^+[RhCl_4{\cdot}nH_2O]^-$, generated from $RhCl_3{\cdot}3H_2O$, Aliquat 336, and $Si(OMe)_4$, also catalyzed the hydrogenation of aryl fluorides and chlorides at 80 °C and 1 atm of H_2 to give halogen-free hydroaromatics.[329] Fluorobenzenes initially yielded fluorocyclohexanes, which eliminate hydrogen fluoride, in a noncatalytic process, followed by hydrogenation of the cyclohexenes. In contrast, chlorobenzenes were first dehalogenated to the corresponding benzene derivatives, which in a second step were hydrogenated to cyclohexanes. Aryl bromides also underwent dehalogenation and hydrogenation but only in the presence of a free radical scavenger. The catalyst was leach-proof and recyclable with little or no loss of activity.

Angelici et al. have tethered rhodium homogeneous catalysts to a silica surface that also supports a second metal such as palladium as a heterogeneous catalyst (Figure 1).[330a,b] These systems showed enhanced synergistic reactivity for the hydrodehalogenation of aromatic fluorides. Thus, fluorobenzene and 1,2-difluorobenzene were defluorinated under very mild conditions (70 °C and 4 atm of H_2 in heptane−ethanol) in the presence of sodium acetate, the heterogeneous catalysts containing the rhodium pyridylphoshine **232** and bipyridyl **233** complexes [Rh(COD)(**232**)]BF_4 and [Rh(COD)(**233**)]BF_4 tethered to heterogeneous silica-supported palladium (Pd/SiO_2).[330c,d] Cyclohexane was the main reaction product, demonstrating that fluorine was removed before the benzene ring was hydrogenated. A reasonable postulate for the enhanced reactivity of these systems is that the aromatic ring of the substrate is activated by coordination to rhodium while hydrogen activation by supported palladium generates highly active hydrogen atoms on the silica surface available for carbon−fluorine and aromatic ring reduction.

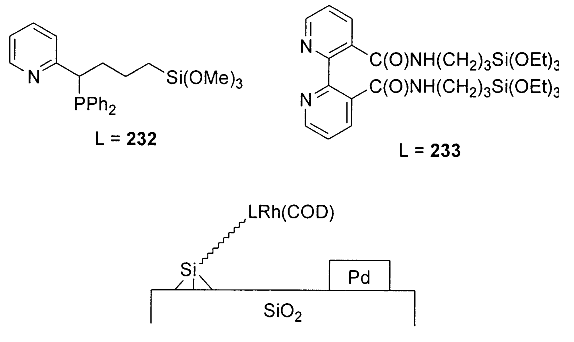


Figure 1. Tethered rhodium complexes on Pd/SiO_2.

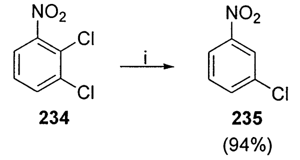
3. Palladium

Among the different transition metals, palladium is the one most frequently used in organic synthesis, a field which has recently achieved a remarkable role due to the manifold and unique transformations that it is capable of mediating, often in a catalytic mode.[331] As previously mentioned, palladium is the most used transition metal in hydrodehalogenation reactions, a topic which is going to be divided into two parts, the first one dedicated to homogeneous processes and the second and major one to tackling the heterogeneous processes.

Although hydrodehalogenations under homogeneous conditions can be accomplished using different sources of hydrogen, the direct homogeneous hydrogenation[332] using molecular hydrogen and a catalytic amount of a soluble palladium complex is still preferred by some research groups. For instance, the selective hydrogenolysis of CFC-113a (CF_3CCl_3) to give HCFC-123 (CF_3CHCl_2), previously described with ruthenium and rhodium complexes, was also achieved with the palladium complex $PdCl_2(Ph_3P)_2$, under 8 atm of molecular hydrogen in THF at 100 °C for 5 h (90% conversion).[309]

Tetrakis(triphenylphosphine)palladium [$Pd(Ph_3P)_4$] was shown to be an efficient catalyst for the selective dechlorination of 2,3-dichloronitrobenzene (**234**) into 3-chloronitrobenzene (**235**) by heating from 20 to 120 °C under 1 atm of hydrogen (Scheme 84).[333] A maximum selectivity of 94% was achieved, 3-chloronitrobenzene being later transformed into nitrobenzene, 3-chloroaniline, or aniline, depending on the catalyst concentration.

Scheme 84[a]



[a] Reagents and conditions: i, $Pd(Ph_3P)_4$, H_2 (1 atm), KOAc, DMF, 20−120 °C, 4 h.

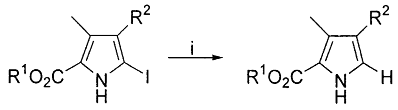
The complex $PdCl_2(Ph_3P)_2$, in combination with an extra amount of triphenylphosphine, was utilized by Toniolo et al. for the hydrodechlorination of α-chloroacetophenone to acetophenone by hydrogen transfer from the H_2O−CO system.[334] The reaction was carried out in ethanol or dioxane at 50−70 °C and 40−80 atm for 2 h with 70−80% yield. Extensive decomposition to metallic palladium was observed when the catalyst precursor was employed without adding an additional amount of triphenylphosphine, the reaction rate increasing with increasing concentration of the catalyst, carbon monoxide pressure, and temperature. It was proposed that the reaction proceeded through the intermediacy of species of the type $Pd(CH_2COPh)Cl(Ph_3P)_2$ [from the oxidative addition of α-chloroacetophenone to Pd(0)], and that $PdCl_2(Ph_3P)_2$ was reduced to the palladium(0) complex by intercalation of CO and H_2O with the metal center to give species containing a Pd−(CO_2H) moiety, which after β-hydride abstraction would generate palladium hydride species with concomitant evolution of CO_2. The hydride would give off a proton and would reduce Pd(II), returning Pd(0) species to the catalytic cycle. It was also found that the complex $Pd(CH_2COPh)Cl(Ph_3P)_2$ was reduced to a Pd(0) complex with formation of acetophenone by the action of H_2O and CO via species of the type H−Pd−(CH_2COPh).

Formates are another source of hydrogen utilized in the palladium-catalyzed homogeneous hydrodehalogenation of organic halides. Thus, water-soluble palladium(II) complexes of the type $PdCl_2(phosphine)_2$ with sulfonated phosphines as ligands catalyzed the dehalogenation of allyl or benzyl halides by means of formates in a biphasic water−heptane system.[335] The reaction was promoted by addition of polyethers of different types as phase-transfer catalysts. Enhancement of the reaction rate and control of selectivity were investigated in the reductive conversion of (*E*)-$PhCH{=}CHCH_2Cl$ to (*E*)-$PhCH{=}CHCH_3$ and $PhCH_2CH{=}CH_2$. Aryl chlorides could be catalytically dechlorinated with sodium formate and $Pd(dippp)_2$ [dippp = 1,3-bis(diisopropylphosphino)propane] in ethanol or DMF.[336]

The formylation of aryl halides with carbon monoxide and potassium or ammonium formate in the presence of $PdCl_2(Ph_3P)_2$ was found to lead to considerable amounts of the reduction products together with minor amounts of the expected aldehydes.[337] For instance, *p*-bromobiphenyl and *o*-bromochlorobenzene gave biphenyl and chlorobenzene in 70% and 79% yield, respectively.

5-Iodopyrroles **236** were smoothly deiodinated with sodium formate and a catalytic amount of either $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$ in DMF at 110 °C to furnish the corresponding 5-unsubstituted pyrrole-2-carboxylates **237**, useful precursors in porphyrin synthesis, in yields ranging from 78% to 88% (Scheme 85).[338]

Scheme 85[a]



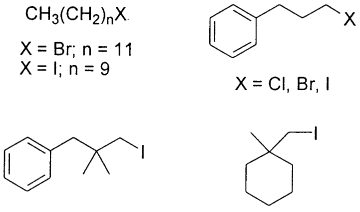
236 **237**

(78-88%)

R^1 = Bn, R^2 = $(CH_2)_2CO_2Me$
R^1 = Et, R^2 = Et
R^1 = Bu^t, R^2 = Me

[a] Reagents and conditions: i, $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$, HCOONa, DMF, 110 °C.

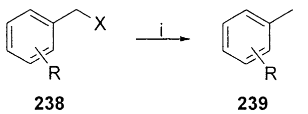
Chart 25. Primary Halides Reduced with EtMgBr and (dppf)$PdCl_2$ at −78 °C to rt for 4−6 h, Followed by Heating at 75 °C for 8−12 h (90−100%)



In the early 1990s Scott et al. reported the hydrodehalogenation of primary alkyl halides (chlorides, bromides, and iodides) with Grignard reagents in the presence of catalytic amounts of (dppf)$PdCl_2$ or (dppf)-Pd(0) [dppf = 1,1′-bis(diphenylphosphino)ferrocene] (Chart 25).[339] The reaction pathway was dependent on the solvent and Grignard reagent used. Thus, in tetrahydrofuran at room temperature or above, reduction was independent of palladium, the alkyl halide being largely reduced by β-hydride transfer from the Grignard reagent, or in some extent by halogen−metal exchange (above all with Grignard reagents without β-hydrogens) followed by protonation. In tetrahydrofuran at low temperatures or in diethyl ether at all temperatures, reduction was very slow in the absence of palladium catalysts, whereas addition of (dppf)$PdCl_2$ markedly accelerated the rate of reduction. Palladium was proposed to act in two competing processes, accelerating both halogen−metal exchange and β-hydride transfer from the Grignard reagent, the latter through a catalytic cycle involving oxidative addition of the alkyl halide, hydride-transfer, and reductive elimination steps.

Diethylzinc was used as reducing agent in the palladium-catalyzed reduction of benzylic chlorides and bromides **238**. Reactions were performed with 1 equiv of diethylzinc and $Pd(Ph_3P)_4$ (1 mol %) as catalyst, in DMF and at room temperature, the reaction going to completion in short times (0.5−1 h) (Scheme 86).[340] This method was compatible with several functional groups on the aromatic ring, including reducible groups such as nitro, cyano, or ethoxycarbonyl. From the results obtained, other mechanistic pathways different from that initially considered, involving hydride transfer from diethylzinc and palladium hydride species, could not be ruled out.

Scheme 86[a]



238 **239**

(0-98%)

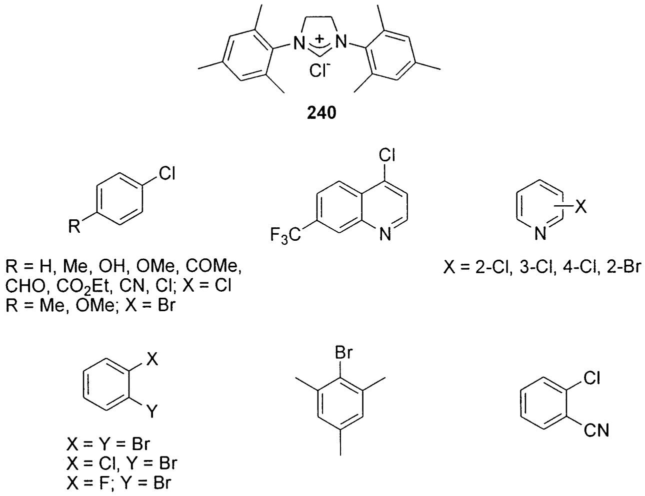
X = Cl, Br
R = Bu^t, MeO, NO_2,CO_2H, CO_2Et, CN, Br

[a] Reagents and conditions: i, Et_2Zn, $Pd(Ph_3P)_4$, DMF, 25 °C, 0.5−1 h.

Hartwig et al. carried out an interesting study on the competitive formation of arylamines and arenes during the palladium-catalyzed amination of aryl halides, resulting from reductive elimination and β-hydrogen elimination, respectively, from a common amido aryl intermediate (obtained by aryl halide oxidative addition).[341] The increasing amounts of arene observed for reactions conducted with increasing quantities of palladium(II) catalyst suggested that some arene was formed either directly or indirectly from reduction to palladium(0) of palladium(II). Reactions catalyzed by complexes containing phosphines with increasing steric demand, involving amides with increasing nucleophilicity and steric demand, and involving palladium-bound aryl groups with decreasing electron density, led to higher ratios of arylamine to arene product.

More recently, Nolan et al. developed an effective protocol for the dehalogenation of aryl chlorides and bromides and polyhalogenated aromatic hydrocarbons, based on the combination of the imidazolium salt (2,4,6-trimethylphenyl)dihydroimidazolium chloride (**240**), with Pd(dba)$_2$ and a base (Chart 26).[342]

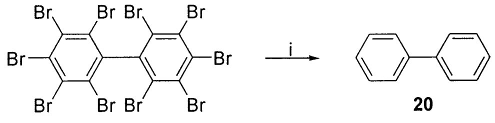
Chart 26. Catalytic Dehalogenation of Aryl Halides with Pd(dba)$_2$, KOMe, and 240 in Dioxane at 100 °C for 1 h (21−100%)



Reactions were performed readily in dioxane at 100 °C, carbon−fluorine bonds remaining unaltered. Strong bases having β-hydrogens both performed deprotonation of the imidazolium salt and were hydrogen sources for the dehalogenation process. A cationic palladium hydride was proposed as the intermediate in the catalytic cycle, generated by an oxidative addition of the imidazolium salt.

A really efficient palladium-catalyzed reductive dehalogenation of polyhalogenated aromatic compounds with sodium borohydride as reducing agent has been extensively studied by Hor et al. In a preliminary study, the complete conversion of hexabromobenzene (chosen as a model compound for degradation of PCBs) to benzene at room temperature with sodium borohydride in the presence of catalytic amounts of PdCl$_2$(dppf) or PdCl$_2$(dppr) [dppr = 1,1′-bis(diphenylphosphino)ruthenocene] and TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) as a base was reported.[343a] Satisfactory efficiencies of 81% and 88% for PdCl$_2$(dppf) and PdCl$_2$(dppr), respectively, were achieved in 1 h, the former increasing the yield up to 100% after 7 h. Similar complete conversions were observed for 1,2,4,5-tetrabromobenzene, 1,3,5-tribromobenzene, 1,2,4-tribromobenzene, 1,2-dibromobenzene, 1,4-dibromobenzene, 1,3-dibromobenzene, and bromobenzene to benzene. This reducing system with a low concentration of the complex PdCl$_2$(dppf) (3.5 mol %) was extended to the hydrodebromination of 4-bromobiphenyl, 4,4′-dibromobiphenyl, and decabromobiphenyl (**241**), giving biphenyl (**20**) (100%) at room temperature in 4 min, 10 min, and 40 h, respectively (Scheme 87).[343b]

Scheme 87[a]



241

20
(100%)

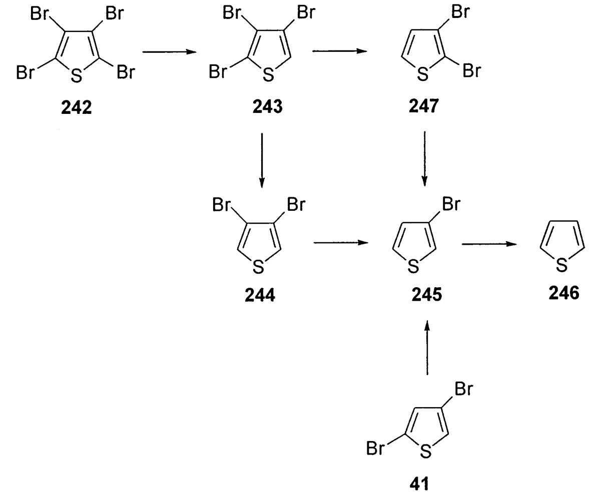
[a] Reagents and conditions: i, NaBH$_4$, PdCl$_2$(dppf), THF, TMEDA, rt, 40 h.

The system NaBH$_4$−PdCl$_2$(dppf)−TMEDA in THF was also utilized in the dehalogenation of the highly chlorinated hexa-, penta-, and tetrachlorobenzenes, total conversion to less chlorinated isomers being achieved within 200 h.[343c] A selective removal of chlorine atoms at the *meta*-positions was preferred over the removal of those at the *ortho*- and *para*-positions. The catalytic activity was found to be strongly solvent-dependent, DMA and DMF showing the best performance.[343d] The effectiveness of the method was tested on the PCB mixtures Arochlor 1242, 1248, and 1254, dechlorination at 67 °C being satisfactory.[343c]

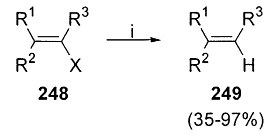
The same authors found this methodology applicable to the synthesis of isomerically pure bromothiophenes and bromobithiophenes.[73,343e] In this case, a palladium-catalyzed hydrodebromination of 2,3,4,5-tetrabromothiophene (**242**), in which the degree of hydrodebromination was controlled by the amount of the reductant sodium borohydride, allowed the synthesis of 2,3,4-tribromothiophene (**243**), 3,4-dibromothiophene (**244**), 2,3-dibromothiophene (**247**), 3-bromothiophene (**245)**, 3,3′,5-tribromo-2,2′-bithiophene, 3,3′-dibromo-2,2′-bithiophene, and 3-bromo-2,2′-bithiophene (Scheme 88). In the presence of a 2−3-fold excess of sodium borohydride, all bromothiophenes and bromobithiophenes were completely debrominated. For all of them, a mechanistic cycle based on oxidative addition, hydride transfer, and reductive elimination was proposed.

Palladium-catalyzed hydrodehalogenations have also been accomplished with other hydrides such as TBTH or triethylsilane. For instance, alkenyl iodides and bromides **248** were reduced with TBTH in the presence of a catalytic amount of Pd(Ph$_3$P)$_4$ to give the corresponding hydrocarbons **249** stereoselectively, with retention of the original stereochemistry except in one case (Scheme 89).[344] Alkenyl iodides reacted easily at 25 °C, whereas alkenyl bromides needed heating at 75 °C for the reaction to go to completion. The method was also successfully applied to the reduction of aryl iodides. As an example,

Scheme 88. Synthesis of Isomerically Pure Bromothiophenes and Thiophene by Controlled Hydrodebromination with $NaBH_4$ and $Pd(Ph_3P)_4$ in MeCN at 70 °C for 3−22 h (70−100%)



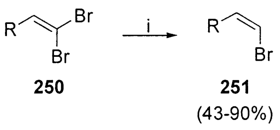
Scheme 89[a]



R^1 = H, Bu^t, n-C_5H_{11}, n-C_6H_{13}, n-$C_{10}H_{21}$
R^2 = H, n-C_5H_{11}, n-$C_{10}H_{21}$
R^3 = H, Bu^t, n-C_5H_{11}, n-C_7H_{15}, n-$C_{10}H_{21}$,
$SiMe_3$, $SiMe_2Ph$, CH_2SPh
X = Br, I

[a] Reagents and conditions: i, $Bu^n{}_3SnH$, $Pd(Ph_3P)_4$, PhH, 25 °C (or 75 °C), 1−5 h.

Scheme 90[a]



R = alkyl, cycloalkyl, aryl, heteroaryl,
vinyl, benzyl, 1,3-dienyl, alkynyl

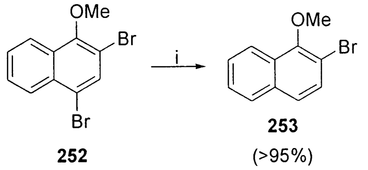
[a] Reagents and conditions: i, $Bu^n{}_3SnH$, $Pd(Ph_3P)_4$, PhH (or PhMe), rt, 0.1−3.5 h.

1-iodonaphthalene was reduced to naphthalene in 94% yield at 25 °C for 5 h.

The same reducing system was elegantly utilized by Uenishi et al. for the stereoselective hydrogenolysis of 1,1-dibromoalkenes **250** to give the corresponding (*Z*)-1-bromo-1-alkenes **251**, important building blocks for (*Z*)-alkene synthesis (Scheme 90).[345] A wide range of 32 different 1,1-dibromoalkenes were subjected to palladium-catalyzed hydromonodebromination with TBTH at room temperature in short reaction times and moderate to excellent yields, triphenylphosphine being the best ligand. The reaction and its selectivity were explained in terms of a highly stereoselective oxidative addition of the carbon−bromine bond located at the *trans*-position of **250** to Pd(0), forming an alkenylpalladium bromide, followed by transmetalation with TBTH to generate an alkenylpalladium hydride, and final reductive elimination to give **251** and regeneration of the Pd(0) species.

The palladium-catalyzed reduction of aromatic halides was also achieved using triethylsilane under microwave irradiation.[346] Reactions could be performed with the complexes $PdCl_2(Ph_3P)_2$ or $PdCl_2[P(o\text{-tol})_3]_2$, but the best results were obtained with palladium(II) chloride in acetonitrile under 490 W of irradiation. Aryl iodides and bromides were quantitatively dehalogenated in 7 min, whereas aryl chlorides reacted moderately, no reaction being observed for aryl fluorides. This method was compatible with the presence of different functionalities such as ketone, ester, or nitro groups, selectively reducing in the same molecule one of two different bromides (see for instance Scheme 91).

Scheme 91[a]



[a] Reagents and conditions: i, Et_3SiH, $PdCl_2$, MeCN, 490 W, 8 min.

Polymer-anchored monometallic or bimetallic palladium-based catalysts[116] proved to be very efficient homogeneous catalytic dehalogenation systems in which the bimetallic synergistic effect can enhance reaction rates and selectivity.[347] These systems were introduced by Liao et al. in the mid-1990s by preparing a palladium anchored on poly(*N*-vinyl-2-pyrrolidone) (PVP−$PdCl_2$). This soluble catalyst exhibited very high catalytic activity for the hydrodehalogenation of organic halides, using molecular hydrogen under atmospheric pressure at 65 °C in absolute ethanol and in the presence of a base, NaOH being the most suitable base, with which the reaction rate was fast and the catalyst stable.[347a] Chlorobenzene, bromobenzene, *m*-dichlorobenzene, *p*-dichlorobenzene, 1,2,4-trichlorobenzene, and benzyl chloride were hydrodehalogenated with high conversion. Ethanol was also demonstrated to be a hydrogen donor in this reaction; thus, iodobenzene was reduced to benzene in the absence of molecular hydrogen. However, a low rate and conversion were observed for chlorocyclohexane. Hydrodechlorination of *p*-chloronitrobenzene to nitrobenzene and then to aniline was also achieved under the above-mentioned conditions.[347b] Hydrodechlorination of hexachlorobenzene using different alcoholic solvents as hydrogen sources showed a contribution of hydrogen following the sequence 1-propanol > ethanol > 2-propanol > water, this contribution being higher with increasing reaction temperature.[347c] On the other hand, polymer-supported bimetallic catalysts such as PVP−$PdCl_2$−$RuCl_3$ increased the rate and selectivity, relative to those of the monometallic catalyst, for some aliphatic bromides,[347d,e] the same behavior being observed for a Pd−Co catalyst supported on PVP in the hydrodechlorination of hexachlorobenzene[347f,g] and chlorobenzene.[347h] Complete hydrodechlorination of chlorobenzene with the homogeneous polymer-anchored catalyst PVP−$PdCl_2$ in NaOAc−EtOH under 0.1 MPa of hydrogen at 65 °C was effected by others.[348]

The catalytic behavior of PVP-supported bimetallic catalysts, made of $PdCl_2$ and other metal salts for the dehalogenation of organic halides, was also studied but with sodium formate as hydrogen-transfer reagent.[349] As a result of a synergistic effect, it was found that samples of PVP−$PdCl_2$−$CdCl_2$ and PVP−$PdCl_2$−$HgCl_2$ exhibited much higher catalytic activity and dechlorination selectivity than PVP−$PdCl_2$, yields of the coupling products being decreased. For instance, when *p*-chloroaniline was used as substrate, the reaction time was shortened to 1/8 of the original time, and the yield of dechlorinated product was about 25 times higher than the original one. On the other hand, when *p*-chlorotoluene was the substrate, the yield of coupling byproduct catalyzed by the bimetallic catalyst was 1/390 of that catalyzed by the monometallic catalyst.

Up to this point of the review we have been aware that catalytic hydrodehalogenation is one of the most promising methods for detoxification of hazardous halogenated organic compounds. Although a variety of catalytic systems have been described, palladium catalysts are in many cases the best choice to cleave the carbon−halogen bond due to their optimal catalytic properties. From an industrial point of view, heterogeneous catalysts have the inherent advantage of being stable, reusable, and easy to separate. Heterogeneous palladium catalysts, and especially supported palladium catalysts, can be used in both the liquid and gas phases and have found application not only in fine chemical synthesis[350a] but also in the development of environmental catalytic technologies,[350b] many of them based on hydrogenolysis of organohalogen compounds.[350c]

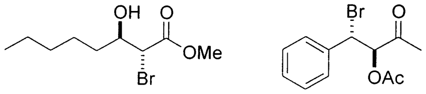
It must be taken into account that supported palladium catalysis is a surface phenomenon, therefore dependent on factors such as particle size and surface area, metal−support interaction, or coexistence with another metal, among others.[177] On the other hand, a wide variety of hydrogen sources can be used, such as molecular hydrogen or hydrogen donors including inorganic salts (phosphinates), organic salts (formates), alcohols, proaromatic compounds, etc. Although hydrogen-transfer reactions proceed, in general, under milder conditions, more acceptable and economical for industry is the use of molecular hydrogen. The interest emerged during recent years in hydrodehalogenation reactions involving heterogeneous hydrogenation[351] catalyzed by supported palladium is reflected in the large number of publications appearing on this topic. Carbon and alumina are by far the most used supports, although other supports as well as bimetallic systems will also be treated.

For instance, Simakova et al. studied the reaction rate of the carbon−chlorine bond hydrogenolysis of different substrates over a Pd/C catalyst, the following trend being reported: $PhCH_2Cl > PhCl > ClCH_2CO_2H >$ decyl chloride. This behavior was explained in terms of the effect of unsaturation on the dissociative adsorption of the substrate on the palladium surface.[352]

A Pd/C catalyst, doubly poisoned with pyridine and a metal ion (Cu^{2+}, Pb^{2+}, As^{3+}) allowed the selective liquid-phase hydrodechlorination of the olefinic compound 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one, preventing the reduction of the carbon−carbon double bond. A synergistic effect was observed for the two types of catalyst poison, the selective poisoning being explained in terms of partial covering of palladium active sites by metal deposition.[353]

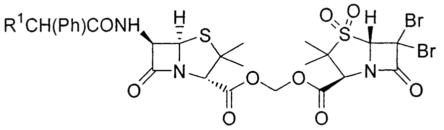
As an example of the synthetic utilities of the above-mentioned methodology, α-bromo-*β*-hydroxy ester **254** and α-acetoxy-*β*-bromide **255**, derived from the corresponding dihydroxy esters, were easily and selectively hydrogenolized by Sharpless et al. under 1 atm of molecular hydrogen at room temperature, with catalytic amounts of 5% Pd/C in EtOH−NaOAc, to give the expected debrominated products in 88% and 79% yield, respectively (Chart 27).[354]

Chart 27



254 **255**

A series of *β*-lactamase inhibitors, used in the treatment of bacterial infections, were prepared by treating the methanediol esters of dioxopenicillanic acid **256** with hydrogen in aqueous EtOAc containing $NaHCO_3$ and a catalytic amount of Pd/C. Under these conditions, double hydrodebromination of the dibrominated starting materials was observed in moderate yields.[355]

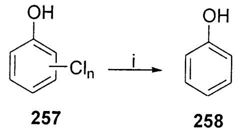


256

$R^1 = NH_2$, $NH(Me)C{=}CHCOR^2$
$R^2 = NH_2$, alkoxy

Allen et al. dechlorinated chlorinated benzenes and chlorophenols in the gas phase over Pd/C catalysts, but in general, elevated temperatures, pressure, or both were required for the mechanism to operate.[292b,356] Balko et al. reported the complete destruction (≥98%) of chlorinated solvents,[357a] chlorophenols[357b] **257**, and chlorobenzenes,[357c] by hydrodechlorination over Pd/C under relatively mild reaction conditions.[357d,e] When hydrogen was used as the reducing agent, all chlorophenols investigated were cleanly hydrodechlorinated to phenol (**258**) at 35 °C and 35 psi in ethanol (Scheme 92). A base was required for the reaction to occur, ammonium hydroxide being superior to the other ones tested. In general, increasing the degree

Scheme 92[a]



257 **258**
n = 1-5 (>98%)

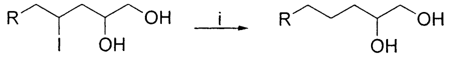
[a] Reagents and conditions: i, H_2 (35 psi) (or hydrazine), 5% Pd/C, EtOH (or EtOH−H_2O), NH_4OH, 35 °C (or rt), 0.5−6 h (or 21−28 h).

of chlorine substitution decreased the rate of dechlorination. 4-Chlorophenol could be dechlorinated in water as solvent due to its solubility. When hydrazine was used as reducing agent, all chlorophenols were dechlorinated to phenol at room temperature without the need for a pressure apparatus, except pentachlorophenol, which required 50 °C. Similar results were obtained for chlorinated benzenes using ammonia as proton acceptor.

Activated carbon cloths as supports for palladium catalysts exhibited good activity and selectivity in the hydrodechlorination of *p*-chlorophenol in the temperature range 30−85 °C. Analysis of the kinetics and diffusion as well as several simulations of adsorption, diffusion, and reaction were presented, showing the effect of pellet size, hydrogen pressure, and adsorbent loading.[358] An increase in the hydrodechlorination rate of chlorobenzene in the liquid phase on Pd/C catalysts was observed by the addition of hydrochloric acid to the reaction medium. A partial oxidation of palladium particles by HCl was rationalized to explain this behavior.[359]

Catalytic hydrogenolysis of carbon−iodine bonds in the presence of other carbon−halogen bonds or functional groups has also been accomplished using palladium on carbon catalysts. For instance, fluorinated 1,2-diols **260** were prepared from the iodinated precursors **259** by catalytic hydrogenation with Pd/C in methanol and in the presence of sodium bicarbonate (Scheme 93).[360]

Scheme 93[a]



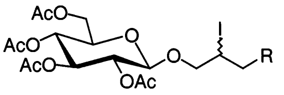
259 **260**

R = C_4F_9, C_6F_{13}, C_8F_{17}
n = 2, 4

(62-80%)

[a] Reagents and conditions: i, H_2, 5% Pd/C, MeOH, $NaHCO_3$, rt, 6 d.

Besides TBTH,[132] Miethchen et al. used hydrogen in the presence of a Pd/C catalyst also to accomplish the hydrodeiodination of perfluoroalkylated carbohydrates **261** in 77−86% yield.[361] The products thus prepared, previous deacetylation, belong to a new group of compounds showing thermotropic liquid-crystalline properties.

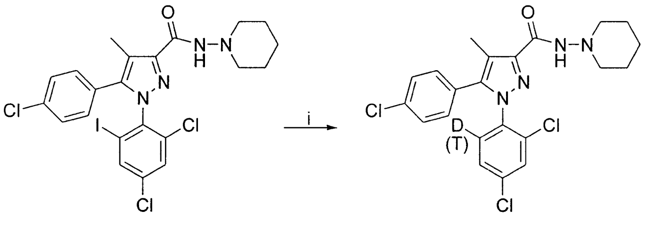


261

R = C_4F_9, C_6F_{13}, C_8F_{17}, $C_{10}F_{21}$

In another example, selective reduction of cannabinoid antagonist SR141716A (**262**) under a deuterium or tritium atmosphere in the presence of 10% Pd/C and triethylamine (Et_2O, 25 °C) led to the corresponding labeled and not overreduced products **263** (Scheme 94).[363,364]

Scheme 94[a]



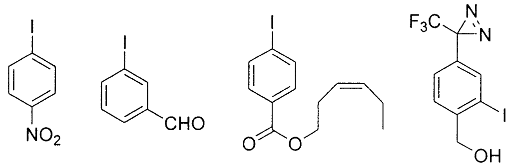
262 **263**

(>93%)

[a] Reagents and conditions: i, $^2H_2$ (or $^3H_2$), 10% Pd/C, Et_2O.

Highly chemoselective hydrogenolysis of iodoarenes using Pd/C and hydrogen was reported by Rousseau et al.[365] It was observed that when an iodoaryl compound and an olefin were separately subjected to these reducing conditions, the double bond was transformed faster. However, when these two groups were reacted together, either belonging to the same molecule or not, the less reactive iodoarene was selectively reduced while the more reactive double bond was unaffected. This selectivity was explained in terms of a marked adsorption of the aryl iodide on the catalyst, thereby preventing access to the olefin. Chemoselective hydrogenolysis of the carbon−iodine bond occurred not only in the presence of carbon−carbon double bonds but also with nitro, aldehyde, or diazirine functionalities with >97% yield (Chart 28).

Chart 28. Chemoselective Deiodination of Iodoarenes with H_2 (1 atm), Pd/C, Et_3N, and MeOH at rt for 50−600 min (>97%)



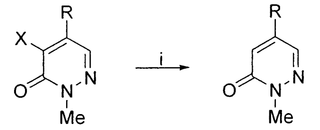
Both batch and continuous experiments have been developed by Rossi et al. for the reductive dehalogenation of PCBs[366a,b] and TCE[366c] by using palladium on carbon catalysts. On a batch process, high conversion of PCBs to hydrocarbons was achieved at 140 °C and 6 bar of H_2, the main limitation being the strong poisoning effect of hydrogen chloride.[366a] By using 0.5% Pd/C in a fixed bed reactor at hydrogen atmospheric pressure and 200 °C, 92% dechlorination of Arochlor 1240 was obtained in the absence of a hydrogen chloride acceptor, with excellent selectivity to biphenyl (90%).[366b] More effective dechlorination was observed in the presence of ammonia, albeit with a concomitant decrease in activity. The hydrodechlorination of TCE was also effected under mild conditions either on water solution or preadsorbed on the carbon-supported catalyst, with the additional advantage of an easy regeneration process based on a low environmental impact technique.[366c]

Seoane et al. described the preparation of several catalysts containing 1% Pd/C by incipient wetness impregnation of the support with H_2PdCl_4 or $Pd(NO_3)_2$, followed by reduction at different temperatures.[367a] Pd(0) and Pd^{n+} species were detected on the catalyst surface, their proportion depending on the reduction temperature and nature of the palladium precursor. All catalysts tested proved to be active and selective in the hydrodechlorination of CCl_4 to $CHCl_3$, though a better selectivity was observed for samples prepared from H_2PdCl_4. A maximum activity was found for a 1:1 Pd(0):Pd^{n+} ratio, assuming that CCl_4 was adsorbed and activated on Pd^{n+} sites, and hydrogen was adsorbed and dissociated on Pd(0) sites. The same research group reported a comparative study on the hydrodechlorination of CCl_4 to $CHCl_3$ in the liquid phase using different metal-supported catalysts.[367b] The hydrodechlorination activity of carbon-supported catalysts followed the order Pd/C > Pt/C > Rh/C > Ru/C > Ni/C. In addition, Pd/C showed a higher activity and selectivity toward $CHCl_3$ than Pd/SiO_2, Pd/Al_2O_3, and Pd/sepiolite, all of them leading the reaction toward hexachloroethane.

Carbon-supported palladium catalysts were found to promote not only hydrodechlorination of CCl_4 but also carbon–carbon bond formation when a flow-type system in vapors under 150–230 °C was used. Hydrodechlorination products were formed together with saturated and unsaturated hydrocarbons having a chain length up to C_5.[368]

A series of 1-methyl-5-halo-4-substituted pyridazin-6-ones **264** were dehalogenated with Pd/C under very mild reaction conditions, giving rise to the corresponding 1-methyl-4-substituted pyridazin-6-ones **265** in good to excellent yields (Scheme 95).[369] The reaction was applied to both chlorinated and brominated starting materials.

Scheme 95[a]



264

R = OMe, NHMe, NHEt, OPh, *p*-$MeOC_6H_4O$
X = Cl, Br

265

(69-98%)

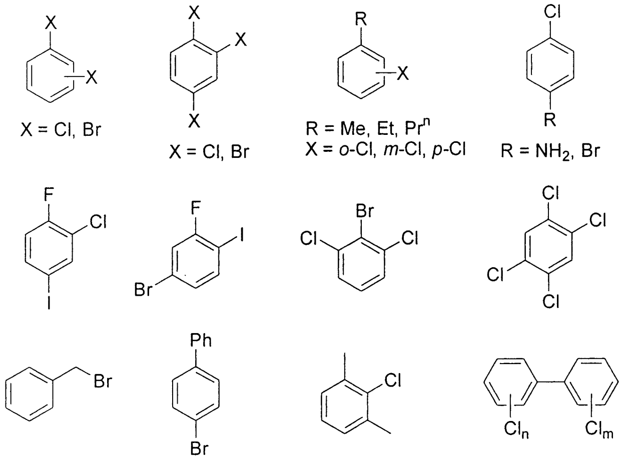
[a] Reagents and conditions: i, H_2 (1 atm), Pd/C, NaOH, MeOH, rt, 2–3 h.

The vapor-phase dechlorination of a mixture of the isomers of trichlorotrifluorobenzene, by hydrogen on 2% Pd/C catalyst and at high temperatures (250 and 300 °C), proceeded with acceptable or good conversions but with a low yield of the desired trifluorobenzenes due to considerable defluorination.[370] However, smooth and selective reductive dechlorination leading to the formation of a mixture of trifluorobenzenes (100% conversion) was achieved when the reaction was conducted in the liquid phase using 1-butanol as solvent, 2% Pd/C as catalyst, and sodium acetate as hydrogen chloride acceptor at 80–90 °C, with only 0.1% reductive defluorination being detected.

The hydrogenolysis of CCl_2F_2 over palladium, platinum, rhodium, ruthenium, iridium, and rhenium on activated carbon was studied by Makkee et al. on a micro flow reactor, in a temperature range of 177–267 °C at 0.4 MPa of hydrogen pressure.[371a–d] Palladium showed a high selectivity for CH_2F_2, iridium and ruthenium for $CHClF_2$, and platinum and rhodium for $CHClF_2$ and CH_2F_2 with moderate selectivity. The adsorption of chlorine on the metal surface played an important role in the selectivity, strong chlorine adsorption leading to a higher selectivity for $CHClF_2$. The results were consistent with a reaction mechanism involving difluorocarbene as the key intermediate. Similar behavior was observed for CCl_3F as starting material, palladium and platinum exhibiting high selectivity for CH_3F, and ruthenium and iridium for $CHCl_2F$.[371e] The palladium-on-carbon-catalyzed transformation of CCl_2F_2 into CH_2F_2 and of $CFCl_2CF_3$ into CH_2FCF_3 was also reported by other groups.[372]

Tundo et al. developed a multiphase system consisting of a hydrocarbon solvent (isooctane), a strong alkaline solution (50% aqueous KOH), and a quaternary onium salt (Aliquat 336), in the presence of a Pd/C catalyst with hydrogen (sodium hypophosphite was formerly used as the hydrogen source)[373a] at atmospheric pressure, which allowed the rapid and progressive displacement of halogen atoms from polyhalogenated benzenes (Chart 29).[373b] In this case, the onium salt constitutes a third liquid phase which contains the supported solid catalyst Pd/C, in which the reaction takes place. Thus, halogenated compounds were partitioned between the hydrocarbon solution and the liquid phase of the phase-transfer agent, rapid removal of hydrogen chloride adsorbed on Pd/C being effected by neutralization with the alkaline solution. A synergistic activation effect was observed for KOH and the phase-transfer catalyst. As an example, 1,2,4,5-tetrachlorobenzene was reduced to benzene under 1 atm of H_2 at 50 °C in 30 min. Selective reduction of aromatic halides was observed in the order ArI > ArBr > ArCl. 2-Chloro-1-fluoro-4-iodobenzene, 4-bromobiphenyl, and Arochlor 1254 were also effectively reduced to benzene and to biphenyl, respectively. The onium salt enhanced both the reaction rates and the regioselectivity in the reduction of isomeric aryl halides.[268,373c] For instance, in the presence of Aliquat 336, isomeric chloroethylbenzenes reacted 50 times faster, and *p*-dichlorobenzene was reduced slower than the corresponding *ortho*- and *meta*-isomers.[373d] In general, Pd/C was more active than Raney Ni on mono- and dihalogenated benzenes; nevertheless, the former can be used to obtain selectively the less halogenated

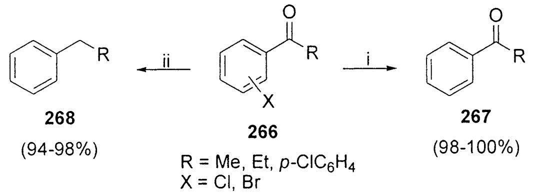
Chart 29. Hydrodehalogenation of Organic Halides under Multiphase Conditions: H_2 (1 atm), 5% Pd/C, Isooctane (or Pentane), 50% KOH, Aliquat 336, 50 °C (or 20 °C)



compounds when highly halogenated aromatics are used as starting materials.[373d]

Hydrodehalogenation with molecular hydrogen and Pd/C catalyst, under the above-described multiphase conditions, was also applied to the selective removal of halogens from aryl ketones **266** without any reduction of the carbonyl group.[321e,f] In contrast, when the reaction was done in the absence of Aliquat 336, the reaction product was the corresponding alkyl benzene **268** (Scheme 96). Moreover, under the same multiphase conditions, only haloaryl alcohols afforded the corresponding aromatic hydrocarbons, whereas nonhalogenated alcohols were reduced only in the presence of an aryl halide as promoter. A series of substituted acetophenones and benzophenones were synthesized by this palladium-catalyzed hydrodechlorination of the corresponding dichlorinated starting derivatives.[373g] More recently, these multiphase conditions were successfully used as a catalytic detoxification methodology for the hydrodechlorination of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans, yielding mixtures where the concentration of contaminants was lower than the experimentally detectable limit.[373h,i]

Scheme 96[a]



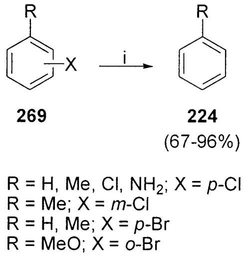
[a] Reagents and conditions: i, H_2 (1 atm), 5% Pd/C, isooctane, 50% KOH, Aliquat 336, 50 °C, 10−45 min; ii, H_2 (1 atm), 5% Pd/C, isooctane, 50% KOH, 50 °C, 30−45 min.

As an alternative to the direct use of molecular hydrogen, Sasson et al. reported the facile and in situ generation of hydrogen gas from water under moderate conditions (35−120 °C) in the presence of zinc powder and catalytic palladium on carbon.[374a] This method was applied to the deuteration of arenes by simple reductive deuteriodehalogenation of haloaromatics. For example, bromobenzene was transformed into deuteriobenzene (72% conversion) with Zn and D_2O at 100 °C for 8 h. When the amount of water (and subsequently the local concentration of hydrogen at the palladium surface) was increased, a higher selectivity for the hydrodehalogenated products was observed, the amount of coupling products being minimized.[374b]

Formates are versatile hydrogen-transfer agents utilized in palladium-on-carbon-catalyzed hydrodehalogenation reactions. For instance, the three isomeric bromoanisoles were reduced with sodium formate in aqueous sodium hydroxide at 60 °C, using 5% palladium on charcoal and cyclodextrins as catalysts.[375] Anisole was the major product though considerable amounts of the corresponding dimethoxybiphenyls were also obtained. It was considered that the reaction predominantly occurred in the aqueous phase, cyclodextrins functioning as inverse phase-transfer catalysts which transport the substrate molecules into the aqueous phase by host−guest complexation.

Sasson et al. studied with more detail the transfer hydrogenolysis of a series of aryl halides **269** by formate salts, performed in ethanol−water with 10% Pd/C at 60 °C (Scheme 97).[376] Both aryl chlorides and bromides were rapidly reduced, ring substituents having a minor effect on the hydrogenolysis rate. High selectivity was observed in the conversion of 4-bromochlorobenzene to chlorobenzene; however, fluorobenzene remained unaffected, and iodobenzene reacted very slowly. The adsorption and activation of the substrate was considered the rate-determining step in the overall transfer hydrodehalogenation process.

Scheme 97[a]



[a] Reagents and conditions: i, HCOOK, 10% Pd/C, EtOH, H_2O, 60 °C, 0.5−1 h.

A mixture of sodium carbonate, formic acid, and 10% Pd/C in aqueous toluene was utilized to reductively dechlorinate 1,2,3,4-tetrachlorobenzene (>98%, 5 min) and PCB Arochlor 1254 (>95%, 60 min) under mild reaction conditions (90 °C).[377] Benzene and biphenyl were the main reaction products, respectively, the latter obtained together with phenylcyclohexane as byproduct.

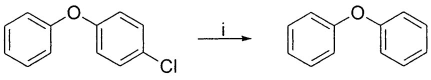
The mechanism of palladium-catalyzed transfer hydrogenolysis of aryl chlorides by formate salts was studied in the mid-1990s by Spatola et al. using chlorotoluene as a model substrate.[378] The hydrogen-donating ability was found to depend on the counterion of the formates, the activity decreasing in the order $Cs^+ \approx K^+ > NH_4^+ > Na^+ > NHEt_3^+ > Li^+ > H^+$. The poor hydrogen-donating ability of formic acid toward aryl chlorides was partly attributed to the deactivating effect of the reaction product hydrogen chloride on the catalyst, but also to the fact that the strong acid HCl led to suppression of the formic acid dissociation, depleting the concentration of formate ions. The latter were considered the active species during the hydrogenolysis, and not formic acid. The kinetic data and isotope effect demonstrated that abstraction of the formyl hydrogen by the catalyst was the rate-determining step, the hydride or hydride-like species generated on the palladium surface reacting with the substrate in a fast step, leading to the hydrogenolized product.

Catalytic transfer hydrogenation of organic halides was also carried out in a 2-propanol solution of sodium hydroxide with Pd/C at temperatures below 82 °C.[379] Aliphatic halides were converted to the corresponding halogen-free hydrocarbons with high yields, although the reaction rate was slower than that of aromatic halides. The dehalogenation rates followed the order RI > RBr > RCl, halogens at terminal positions of the carbon chain being more easily dehalogenated than those at the internal positions.

Metal hydrides in combination with Pd/C were found to be effective reagents for dehalogenation reactions. For instance, LAH−Pd supported on porous carbon was utilized to quantitatively dechlorinate chlorobenzene under mild conditions (22 °C, 6 h).[380a] Reaction with LAH−Pd/C proceeded with conversion (100%) higher than that of other combinations [LAH (5%, 70 °C, 4 h), LAH/C (24%, 70 °C, 4 h)]. ^{27}Al and ^{1}H NMR data provided information on the types of hydride species and their interaction with the support surface, suggesting that the formation of mixed Pd−LAH-supported hydrides might be responsible for the increase of the reactivity. The catalytic system Pd/C−NaH(LAH)$_{1/2}$ also proved to be very active, allowing the quantitative dechlorination of 2,3-dichlorodibenzo-1,4-dioxin at 70 °C.[380b]

Borane−amine complexes, precursors of the abovementioned lithium aminoborohydrides,[76] are also an important class of reducing agents that have found several applications in organic synthesis.[381a] In this context, Couturier et al. recently reported the palladium-induced methanolic cleavage of stable borane−amine complexes, palladium hydride likely being the transient species prior to molecular hydrogen liberation.[381b] The authors took advantage of this result to utilize borane−amine adducts, such as $Bu^tNH_2{\cdot}BH_3$, as palladium-catalyzed hydrogen-transfer reagents in methanol.[381c] Although several representative functional groups were reduced with the $Bu^tNH_2{\cdot}BH_3$−Pd/C−MeOH system, at room temperature in a sealed vessel, *p*-chlorophenyl phenyl ether (**270**), the only organic halide tested, required a long reaction time (120 h) to achieve 82% of the corresponding dechlorinated product (**271**) (Scheme 98).

Scheme 98[a]

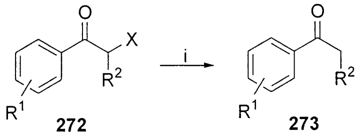


270 **271**
(82%)

[a] Reagents and conditions: i, $Bu^tNH_2{\cdot}BH_3$, Pd/C, MeOH, rt, sealed vessel.

Decaborane ($B_{10}H_{14}$), although less reactive than borane as reducing agent, generates hydrogen gas slowly in a protic solvent. Taking advantage of this property, Yoon et al. described the smooth dehalogenation of α-haloacetophenones **272** with 10% Pd/C in methanol at room temperature (Scheme 99).[382] The process was chemoselective, carbonyl, nitro, or aromatic bromine groups remaining unaffected.

Scheme 99[a]



272 **273**
(91-99%)

R^1 = H, *p*-Me, *p*-Br, *m*-NO_2
R^2 = H, Me
X = Cl, Br

[a] Reagents and conditions: i, $B_{10}H_{14}$, 10% Pd/C, MeOH, rt, 1−12 h.

Alumina is probably the second most used solid support for palladium in hydrodehalogenation reactions, especially applied to the hydrodechlorination of CFCs. Karpinski et al. studied in detail the hydrodechlorination of CF_2Cl_2 (CFC-12) in the presence of similarly dispersed alumina-supported palladium.[383a] It was observed that the catalytic activity of α-Al_2O_3 and γ-Al_2O_3 was not dependent on the type of alumina used as support. However, Pd/α-Al_2O_3 appeared to be more selective toward CH_2F_2 than Pd/γ-Al_2O_3. Since α-Al_2O_3 is a less porous carrier than γ-Al_2O_3, lower selectivity toward partial hydrodehalogenation on Pd/γ-Al_2O_3 was probably due to a consecutive transformation of CH_2F_2 to methane. High-temperature pretreatment supposedly eliminated narrow pores in γ-Al_2O_3, thus leading to higher selectivity to CH_2F_2. A strong dependence on metal dispersion was found, poorly dispersed palladium samples exhibiting the highest turnover frecuencies and selectivities toward the formation of CH_2F_2.[383b] Considerable amounts of carbon found in used catalysts were suggested to affect the properties of Pd/γ-Al_2O_3 by either incorporation of carbon into the palladium lattice or formation of a carbide. In fact, the poorly dispersed palladium catalysts, which are prone to suffer more severe carbiding, led to surfaces which bound CFCs less strongly, therefore resulting in a higher activity and selectivity to partial dehalogenation (e.g., formation of CH_2F_2). At high temperatures (600 °C) a Pd−Al compound was believed to be formed, somewhat increasing the selectivity to CH_2F_2. A series of Pd/γ-Al_2O_3 catalysts were also tested for the hydrodechlorination of CH_2Cl_2, the catalytic behavior resembling in many aspects the behavior described above for CCl_2F_2.[383c] The use of deuterium instead of hydrogen furnished CH_2D_2, CD_4, and CH_2DCl as the main initial products, the ratio of CH_2D_2 to CD_4 following the same trend as that of the palladium dispersion described above; that is to say, low metal-dispersed catalysts showed higher selectivities. Pd/γ-Al_2O_3 also displayed high activity for the hydrodechlorination of 1,1-dichlorotetrafluoroethane ($CFCl_2CF_3$).[383d,e] High hydrogen partial pressures were needed to avoid deactivation, the three main products formed being 1,1,1,2-tetrafluoroethane (CFH_2CF_3), 1-chloro-1,2,2,2-tetrafluoroethane ($CFClHCF_3$), and 1,1,1-trifluoroethane (CH_3CF_3), with approximately 85% selectivity toward the desired product CFH_2CF_3. A very high activity was observed in this reaction with a catalyst pretreatment consisting of reoxidation and subsequent low-temperature reduction of the catalyst, prereduced at 600 °C.

The hydrogenolysis of CCl_2F_2 with Pd/Al_2O_3 xerogel and aerogel catalysts led to $CClF_3$ and CH_4.[384] Carbon incorporation into the palladium lattice and formation of AlF_3 were observed at the initial stage of the reaction, the latter being responsible for the chlorine−fluorine exchange. Methane formation could also be explained by reaction between hydrogen in the gas phase and the interstitial carbon.

Pd/Al_2O_3 catalysts fluorinated by using $CHCl_2F$ (HCFC-22) or reduced by hydrogen were characterized and tested in the hydrodechlorination of CCl_2F_2 (CFC-12). In general, the fluorinated catalyst gave better performance, with a higher activity and selectivity toward the product CH_2F_2 (HFC-32).[385] An improved activity and selectivity toward CH_2F_2 was also observed in the hydrodechlorination of CCl_2F_2 when microwave irradiation was used in the preparation of low dispersed Pd/Al_2O_3 catalysts.[386]

Palladium supported on Al_2O_3, a series of fluorinated Al_2O_3, and AlF_3 were investigated in the gas-phase hydrodechlorination of CF_3CFCl_2 to CF_3CFH_2 and CCl_2F_2 to CH_2F_2.[387] It was found that for CF_3CFCl_2 all catalysts exhibited a rapid and significant decrease in activity, whereas little change in activity with time occurred with CCl_2F_2. The catalyst deactivation during the transient period was rationalized in terms of chlorine (or fluorine) poisoning and carbonaceous species deposition on the palladium surface. Pretreatment of $Pd/\gamma\text{-}Al_2O_3$ with CHF_2Cl (HCHC-22) significantly improved the catalytic activity and catalyst lifetime, the presence of palladium carbide probably enhancing the selectivity to CH_2F_2 and preventing sintering of palladium.[388] Palladium on alumina also showed the best performance in the gas-phase dehalogenation of $CHCl_3$ and CH_2Cl_2 to CH_4, and that of chlorobenzene to benzene, using hydrogen under mild conditions.[389]

Reinhard et al. studied the hydrodechlorination of different organic chlorides using Pd/Al_2O_3 and hydrogen in water. For instance, all chlorinated ethylenes, including tetrachloroethylene and vinyl chloride, were completely removed from tap water within 10 min at room temperature by 0.5% Pd/Al_2O_3 and 0.1 atm of H_2.[390a,b] Ethane accounted for 55−85% of the mass balance in these systems, ethylene being a reactive intermediate whose maximum concentration accounted for less than about 5% of the initial substrate. Palladium on granular carbon was also an effective catalyst, although the ethane yield from tetrachloroethylene was somewhat lower than that with Pd/Al_2O_3 (55% vs 85%). TCE dechlorination with Pd/Al_2O_3 in water was also studied, the aqueous-phase hydrogen concentration and the presence of competitive solutes affecting the dechlorination rate and product distribution.[390c,d] With decreasing aqueous-phase hydrogen concentration, an important decrease in the dechlorination rate constant and increase in the formation of chlorinated intermediates and C_4-C_6 radical coupling products was observed. On the other hand, the TCE transformation rate was practically unaffected by the presence of competing solutes such as *cis*-1,2-dichloroethene, *trans*-1,2-dichloroethene, 1,1-dichloroethene, dissolved oxygen, nitrite, and nitrate at certain concentrations. This methodology was especially useful for chlorine removal from 1,2-dichlorobenzene, chlorobenzene, 4-chlorobiphenyl, and γ-hexachlorocyclohexane (lindane), under very mild reaction conditions (room temperature and atmospheric pressure).[390e] Hydrodechlorination of 1,2-dichlorobenzene to benzene was complete in 13 min. 4-Chlorobiphenyl was quantitatively transformed into biphenyl in 10 min, further reduction leading to dicyclohexyl as the final product, whereas lindane suffered dechlorination in 18 min to give benzene in 99% yield. In contrast, higher temperatures (80−180 °C) were reported by other authors to be needed for the dechlorination of chlorinated benzene and phenols over Pd/Al_2O_3.[391] Successful hydrodechlorination on Pd/Al_2O_3 catalysts of chlorinated substrates such as 1,2-dichlorobenzene,[392] 3-chlorotetrafluoropyridine,[393] or mixtures of chlorobenzene−tetrachloroethylene[394] were reported by other groups.

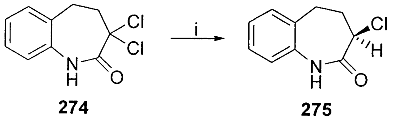
McNab et al. developed a two-stage column to saturate an aqueous phase with hydrogen and allow treatment of groundwater containing chlorinated aliphatic compounds.[395] The first stage consisted of an undivided electrolyzer cell to generate hydrogen by electrolyzing the influent water. The second stage contained a catalyst bed of palladium metal supported on alumina beds. This reactor had removal efficiencies greater than 95% for tetrachloroethylene, TCE, 1,1-dichloroethylene, and carbon tetrachloride with residence times on the order of 2 min. However, chloroform and 1,2-dichloroethane appeared less susceptible to dehalogenation by this process.

As already described in this review, large changes in the carbon isotopic composition of chlorinated ethylenes were observed during the reductive dehalogenation by metallic iron.[223] By using Pd/Al_2O_3, TCE was rapidly dechlorinated to ethane as the final product (metallic iron was less reactive, requiring contact times ranging from hours to days for significant dehalogenation).[396] In general, molecules containing the lighter isotopes reacted preferentially, resulting in an increased enrichment of ^{13}C in the remaining TCE. Therefore, in field applications the difference in carbon isotopic composition values between TCE and the degradation products could serve as a powerful tool to estimate the reaction progress of dehalogenation on palladium catalysts. The same preferential $^{12}C-Cl$ bond cleavage was observed for the microbial reductive dehalogenation reaction.

With all the advantages of performing heterogeneous catalysis in supercritical fluids,[397] Burk et al. reported the first catalytic dechlorination reaction in supercritical carbon dioxide ($scCO_2$).[398] A Pd/Al_2O_3 catalyst was used for the dechlorination of 1-chlorooctadecane with 2-propanol as hydrogen donor in $scCO_2$, the reaction being compared with the dechlorination in 2-propanol at atmospheric pressure. The reaction was observed to proceed faster in $scCO_2$, the addition of sodium hydroxide increasing the yield when the reaction was performed only in liquid 2-propanol, whereas the presence of either sodium hydroxide or triethylamine in $scCO_2$ lowered it. The adsorption of 1-chlorooctadecane on the palladium surface was deduced to be the rate-determining step of the reaction. This study was extended to the dechlorination of 9,10-dichlorostearic acid and 12,14-dichlorodehydroabietic acid.

Palladium on supports different from carbon and alumina has also found application in hydrodehalogenation reactions. For instance, 5% $Pd/BaSO_4$ modified with cinchonine was utilized in an interesting and enantioselective monohydrodehalogenation of α,α-dichlorobenzazepin-2-one (**274**), under 3 bar of H_2 in THF using tributylamine as hydrogen chloride acceptor (Scheme 100).[399] Although the reaction proceeded with excellent conversion and chemoselectivity, very high modifier and catalyst concentrations were necessary to obtain good optical yields (50% ee was the maximum achieved) and reasonable rates, since the modifier decreased the catalytic activity. Unfortunately, attempts to extend this enantioselective dehalogenation to other α,α-dihalogen-substituted acid derivatives were unsuccessful.

Scheme 100[a]



(50% e.e.)

[a] Reagents and conditions: i, H_2 (3 bar), 5% Pd/$BaSO_4$–cinchonine, Bu_3N, THF, 25 °C, 1 h.

Coq et al. studied the hydrodehalogenation of CCl_2F_2 in the gas phase, under atmospheric pressure of hydrogen between 160 and 250 °C over palladium black, palladium supported on alumina, graphite, and aluminum trifluoride.[400a] CH_2F_2 and CH_4 represented more than 95% of the products, Pd/AlF_3 showing the best catalytic properties remaining unchanged with time. In contrast, Pd/graphite, Pd/ Al_2O_3, and Pd black suffered changes of activity and/or selectivity during the first few hours on stream, which was attributed to diffusion of halide species into the bulk of palladium, and transformation of Al_2O_3 to AlF_3. The CH_2F_2:CH_4 selectivity ratio was the lowest on Pd/graphite and the highest (81%) on Pd/AlF_3, adsorbed or absorbed halide species being proposed as responsible for the loss of CH_2F_2 selectivity. The high selectivity ratio on Pd/AlF_3 was rationalized in terms of a metal–support cooperation. Other supports such as titanium and zirconium oxides and fluorides were also studied under the above reaction conditions, the best selectivity (90%) to the desired product CH_2F_2 being reached for Pd/ZrF_4.[400b] The distribution of products was explained by formation of carbenoid surface species.[401]

Two new catalysts based on dichlorobis(triphenylphosphine)palladium (DCTPPP) and dithiocyanatobis(triphenylphosphine)palladium (DTTPPP) complexes supported on MgF_2 exhibited excellent catalytic activities in the hydrodechlorination of CCl_2F_2.[402] In both cases, high selectivities (>85%) of CH_2F_2 formation were achieved, no deactivation being observed within 60 h. The notable properties of these catalysts, including good stability, were primarily attributed to the high dispersion of palladium. A similar performance was observed for supported $PdCl_2/Bu^n{}_4NCl$ molten salts in the above transformation.

The catalytic properties of a series of supported palladium catalysts and the influence of the reaction conditions in the hydrodehalogenation of aryl halides was studied in detail by Urbano et al.[403] The following supports were subjected to study: MgO (basic), ZrO_2 (amphoteric), SiO_2–$AlPO_4$ (high specific surface area and high surface acidity), and SiO_2–$AlPO_4$ modified with NaOH to ensure a sodium content of 5%. Bromobenzene[403a] and chlorobenzene[403b] were chosen as model compounds using molecular hydrogen in methanol at 0.414 MPa and 40 °C. Regarding the activity, Pd/SiO_2–$AlPO_4$ and Pd/MgO exhibited similar turnover frequencies that were slightly higher than that for Pd/ZrO_2. The different acid–base properties of the supports exerted a strong influence on the catalyst deactivation. Thus, ZrO_2 (with bromide species affinity) allowed the reaction to be complete within relatively short times (100% conversion in 990 min for bromobenzene), whereas the MgO support was dissolved as the pH of the reaction medium decreased by the hydrogen halide formed, prematurely stopping the reaction. The activity was found to depend on the metal particle size (the reaction is structure-sensitive), both the initial catalytic activity and the residual conversion being inversely related to metal dispersion. Addition of sodium hydroxide to the reaction medium although had no effect on the initial activity and drove the reaction to completion by avoiding passivation of the catalyst. This study was extended to other halobenzenes using not only molecular hydrogen but also hydrogen transfer from potassium formate and 2-propanol.[403c,d] Hydrogen-transfer competitive reactions with HCO_2K confirmed the strong adsorption of iodobenzene over the catalyst, consequently inhibiting the adsorption of the other aryl halides and the donor. However, when 2-propanol was used as hydrogen donor, not only iodobenzene but also fluorobenzene was easily reduced. Pd/MgO was the best catalyst among all solids tested, demonstrating that the basicity of the support played an important role in the final performance of the catalytic system. Hydrogen gas–liquid-phase catalytic hydrodehalogenation showed the reactivity order PhBr > PhCl > PhI > PhF, according to the carbon–halogen bond dissociation energy and the adsorption strength of the halobenzene. More recently, the same group improved the performance of palladium catalysts by studying the effect of addition of sodium compounds in the hydrodechlorination of chlorobenzene.[403e] Six different supported palladium catalysts (based on SiO_2–$AlPO_4$) and the effect of sodium additives by three different methods were analyzed. Doping the support with sodium hydroxide prior to impregnation with the metal precursor led to catalysts with better activity and tolerance to deactivation, especially those obtained using $PdCl_2$ as the metal precursor. Low metal dispersion and the capture of chloride by forming sodium chloride were suggested to be the main factors contributing to the improved catalytic properties.

Yamanaka et al. studied a wide variety of palladium-supported catalysts to achieve rapid and complete hydrodechlorination of 2,4-dichlorophenoxyacetic acid with hydrogen.[404] Among them, Pd/TiO_2 exhibited the best performance, reaching a high turnover number of Pd at 30 °C. A strong synergism of Pd and TiO_2 was observed, the nature of the interface controlling the hydrodechlorination process. The results obtained suggested that molecular hydrogen dissociatively adsorbs on the interface (competitively with 2,4-dichlorophenoxyacetic acid), the active hydrogen species successively dechlorinating the substrate through 2- and 4-chlorophenoxyacetic acid.[404] However, 1,4-dichlorobenzene was partially hydrodechlorinated in a tube reactor packed with Pd/TiO_2 and heated at 180 °C, giving benzene (32.5%), chlorobenzene (55.7%), and starting material (11.7%).[405]

Palladium supported on ternary oxide catalysts $Pd/TiZrAlO_n$ and $Pd/TiZrSiO_n$ were prepared and their catalytic hydrodechlorination activities evaluated in comparison with the component single-oxide-supported catalysts Pd/TiO_2, Pd/ZrO_2, Pd/SiO_2, and Pd/Al_2O_3.[406] 1,2-Dichlorobenzene was chosen as a model compound, the reactions being performed in the gas phase under atmospheric hydrogen pressure at 200 °C in a micro flow reactor system. Benzene was the major product obtained with the following decreasing order of activity: $Pd/TiZrAlO_n > Pd/TiZrSiO_n > Pd/ZrO_2 > Pd/Al_2O_3 > Pd/TiO_2 > Pd/SiO_2$. In particular, the ternary oxide-based catalyst $Pd/TiZrAlO_n$ exhibited an improved stability and activity much higher than the arithmetic sum of activities of the component single-oxide-based palladium catalysts. This behavior was ascribed either to interaction between the support and the metal or to adsorption of reactants on the support.

Catalysts with improved durability and increased content of palladium were manufactured by impregnating a dry porous support, such as silica gel, with a solution of palladium followed by reduction with hydrogen. These catalysts were especially useful for hydrodechlorination of di- and trichloroacetic acid.[407] Different silica-supported noble metal catalysts were also tested in the hydrodechlorination of CCl_2FCF_3 (CFC-114a), the catalytic activity following the trend Pd > Rh > Pt > Ru. Palladium and ruthenium catalysts gave selectively FCH_2CF_3 and $FCHClCF_3$, respectively, whereas both rhodium and platinum catalysts led to CH_3CF_3.[408]

Schoedel et al. utilized an aluminosilicate as support for palladium catalysts, containing 0.5−8% Pd and 1−50% SiO_2. The catalysts were prepared by impregnation of amorphous aluminosilicate pellets with a $Pd(NO_3)_2$ solution followed by a thermal treatment, and found application in the complete conversion of a mixture of trichlorobenzene isomers to cyclohexane and hydrogen chloride.[409] This type of catalyst allowed the high yield and selective preparation of 2,6-dichlorotoluene by hydrodechlorination of mixtures of polychlorotoluenes in the presence of hydrogen.[410]

Kantam et al. designed a catalyst composed of palladium anchored to the mesoporous material MCM-41 (pure silica), used for hydrodehalogenation of aryl halides with molecular hydrogen at atmospheric pressure.[411] The catalyst was prepared by consecutive calcination of MCM-41 and reflux with 3-triethoxysilylpropylamine, followed by complexation with dichlorobis(benzylcyano)palladium(II).[411a] Hydrodehalogenation reactions were in most cases carried out at room temperature in ethanol, the catalyst being reusable without any loss of activity.[411b] Several aryl chlorides and bromides as well as bromocyclohexane and benzyl bromide suffered hydrodehalogenation in moderate to excellent yields (36−92%).

Catalytic hydrodebromination of aromatic bromides proceeded with remarkable activities and selectivities with palladium catalysts supported on montmorillonite K10 (Mont K10).[412] These catalysts were easily prepared (an amine was used as adsorbent), needed a low amount of palladium, and showed good reusability. The use of polar solvents and the presence of bases was recommended for an optimum catalytic hydrodebromination reaction.

A palladium on zeolite catalyst obtained by Reinhard et al. was utilized for treating groundwater contaminated with halogenated hydrocarbon compounds with dissolved hydrogen. 1,2-Dichlorobenzene and aqueous sulfite were used as model substrate and poison, respectively, the optimal palladium support being a hydrophobic zeolite Y with a pore size of 0.74 nm. A series of chlorinated ethylenes and aromatic derivatives were dehalogenated within minutes.[413]

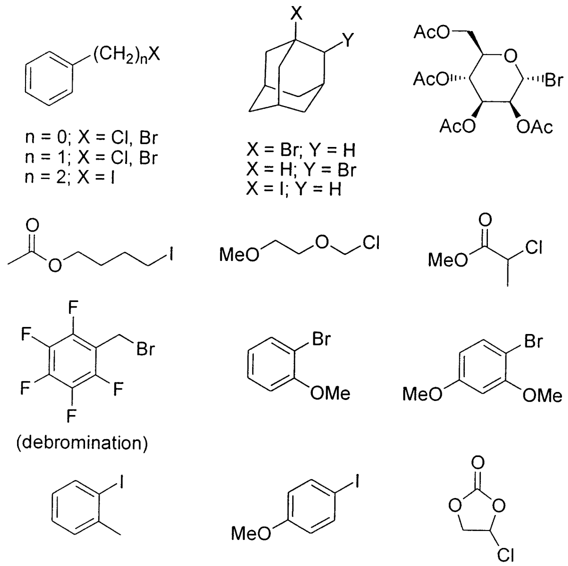
Unsupported monometallic palladium catalysts have been scarcely utilized for hydrodehalogenation reactions; in fact and to the best of our knowledge, only a few examples have been reported in the recent literature. For instance, $Pd(OAc)_2$ was used as catalyst in the hydrodechlorination of CCl_4 with hydrogen, the distribution of products being dependent on the solvent used.[414] Thus, CH_4 was the main product when the reaction was carried out in acetic acid, whereas $CHCl_3$ and CH_3Cl were preferentially obtained in a mixture of acetic acid and *tert*-butyl alcohol.

Beletskaya et al. studied the dehalogenation of bromo and iodo derivatives of phenols, anilines, benzoic acids, and nitrogen-containing heterocycles with the $PdCl_2(cat)-NaBH_4-H_2O-NaOH$ system, which proceeded with quantitative yields to the corresponding aromatic products.[415]

The complex $Pd(hfacac)_2$ (hfacac = $CF_3COCHCOCF_3$), which is soluble in many organic solvents (heptane, Et_2O, CH_2Cl_2, and Me_2CO), can be reduced to a stable brown-yellow colloidal palladium upon addition of silanes. PMHS was found both to reduce the palladium complex and to stabilize the resulting colloid, allowing its regeneration in different solvents. In the presence of either H_2−PMHS or Et_3SiH−PMHS, benzyl chloride, benzoyl chloride, and the three halobenzenes (PhCl, PhBr, and PhI) were dehalogenated at room temperature (for molecular hydrogen) or at reflux (for triethylsilane).[416]

It is known that treatment of organohydrosilanes with haloalkanes in the presence of a catalytic amount of palladium(II) chloride afforded halosilanes in high yields together with the corresponding alkanes.[417] With this premise, Chatgilialoglu et al. used the combination $Et_3SiH-PdCl_2$ as a very efficient reducing system for the dehalogenation of organic chlorides, bromides, and iodides (Chart 30).[418] Except in a few cases, all reductions took place in very short reaction times and at room temperature with excellent yields. In general, chlorides, bromides, and

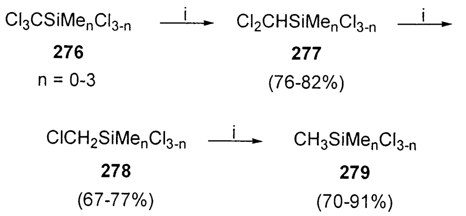
Chart 30. Dehalogenation of Organic Halides with Et_3SiH and $PdCl_2$ at rt (or 80 °C) for 2 min to 24 h (78 to >95%)



iodides behave similarly although certain increasing reactivity in the order RI > RBr > RCl was observed. Three possible reaction mechanisms were proposed to account for the results of different experiments involving (a) free radicals, (b) oxidative addition of the alkyl halide to the metallic palladium in situ generated, or (c) oxidative addition of the silane to the palladium catalyst followed by silyl−alkyl group exchange.

Selective dechlorination of the chloromethyl-containing silanes **276** with Cl_3SiH was studied in the presence of $Pd(OAc)_2$ or $PdCl_2$ as catalyst (Scheme 101).[419] The dechlorination rate was found to increase as the number of chlorine atoms on carbon and of methyl groups on silicon increased. The reactivity difference between (trichloromethyl)-, (dichloromethyl)-, and (monochloromethyl)chlorosilanes allowed the selective stepwise reduction of the $SiCCl_3$ moiety to $SiCHCl_2$, $SiCH_2Cl$, and finally $SiCH_3$, by controlling the amount of trichlorosilane and the reaction conditions. A possible mechanism involving black palladium powder as catalytically active species was proposed.

Scheme 101[a]



[a] Reagents and conditions: i, Cl_3SiH, $Pd(OAc)_2$ (or $PdCl_2$), sealed bomb, 100−150 °C, 4−12 h.

Many efforts have been devoted to study the kinetics and to understand the mechanism of the hydrodehalogenation reaction on solid palladium catalysts.[177,350] An outstanding contribution to this field has been made by Gellman et al., who studied the transition state for the dechlorination reaction on the Pd(111) surface using a set of four substituted 1,1-dichloroethanes (CF_3CFCl_2, CF_3CHCl_2, CH_3CFCl_2, and CH_3CHCl_2), on the basis of the substituent effect methodology.[420a−d] The results suggested that the transition state for the carbon−chlorine bond cleavage is homolytic and occurs early in the reaction coordinate. In this dechlorination reaction it was possible to correlate the kinetics measured on single-crystal surfaces with the kinetics observed on supported palladium catalysts. Under high-pressure reaction conditions, catalytic hydrodechlorination was rate-limited by the dechlorination step and therefore by the same transition state as in the case of the Pd(111) surface. The early transition state observed in the dechlorination reaction was also observed for the carbon−iodine bond cleavage on the Pd(111) surface.[420e] On the other hand, Somorjai et al. studied the hydrodechlorination of CF_3CFCl_2 and CCl_2F_2 on Pd(111) and Pd(110) single crystals and on polycrystalline foils.[421] The latter were observed to be more active than the single crystals, whereas lower deactivation rates and a higher activation energy for CH_2F_2 formation from CCl_2F_2 were found for Pd(111). The differences observed were related to the different capacities to accommodate surface chlorine atoms in the two cases. It could be concluded that the hydrodehalogenation reaction on the palladium surface is not a structure-sensitive reaction and the differences in the catalytic behavior as a function of the palladium particle size, reported by some authors, could be related to other properties which change at the same time.

Finally, we overview some hydrodehalogenation reactions under heterogeneous conditions but involving bimetallic palladium catalysts.[422] It is well-known that catalytic properties of palladium can suffer important alterations by addition of a second metal, the resulting effect depending on many factors such as the chemical state and spatial distribution in the surface layer of the two components, possible surface segregation of one component, or interaction between the two components, among others. In addition, the preparation method will have an important influence on the previous factors. The use of bimetallic palladium combinations emerged as one of the most effective ways to increase degradation rates of halogenated compounds.[211e]

Coq et al. studied the conversion of CCl_2F_2 in the gas phase under an atmospheric pressure of hydrogen, between 140 and 200 °C, over graphite-supported Pd, Pd−K, Pd−Fe, Pd−Co, and Pd−Ag catalysts.[423] At a low CCl_2F_2 pressure, CH_2F_2 and CH_4 represented more than 95% of the products. However, at a high CCl_2F_2 pressure and over Pd−Fe/graphite or Pd−Co/graphite catalysts, high selectivities for the coupling product CF_2CF_2 were obtained. The latter behavior was probably due to the occurrence of some mixed sites between palladium and iron or cobalt. An adsorption competition for the active sites between CCl_2F_2 and hydrogen was observed and ascribed to a halogenation−dehalogenation mechanism of the palladium surface by CCl_2F_2 and hydrogen, respectively.

Catalytic hydrodechlorination of 1,1,2-trichlorotrifluoroethane, CCl_2FCClF_2 (CFC-113), attracted the attention of several research groups, being attempted over different supported metal and oxide catalysts.[288,424] In general, high temperatures were required, low product selectivity and deactivation of the catalysts being the major drawbacks. However, more than 80% selectivity in the hydrodechlorination of 1,1,2-trichlorotrifluoroethane to chlorotrifluoroethene and trifluoroethene was observed over palladium catalysts containing selected metal additives such as Ag, Bi, Cd, Cu, Hg, In, Pb, Sn, and Tl.[425] In particular, a thallium-modified 5% Pd/C and a bismuth-modified Pd/SiO_2 gave chlorotrifluoroethene and trifluoroethene, respectively, with over 90% yield. The high selectivity observed was explained by partial suppression of the hydrogenation activity by the modifier.

To overcome the substantial deactivation of Pd/γ-Al_2O_3 catalysts in the hydrogenolysis of chlorofluorocarbons, Thomson et al. introduced ZnO as a cocatalyst to stabilize the Pd(0) function, leading to a novel γ-alumina-supported palladium catalyst which proved to be active toward the hydrogenolysis of 1,1,2-trichlorotrifluoroethane.[426] Higher conversions (up to 96% at 350 °C) were achieved with $Pd-ZnO/\gamma$-Al_2O_3 in comparison with Pd/C and Pd/γ-Al_2O_3 catalysts, with a 94% selectivity to CH_3CF_3 at 82% conversion. The lifetime of the $Pd-ZnO/\gamma$-Al_2O_3 catalyst was also enhanced relative to that of Pd/γ-Al_2O_3 operating under identical conditions, a synergistic effect being suggested to exist where the presence of palladium stabilizes the zinc oxide function against halogenation and the presence of zinc oxide stabilizes the palladium function against oxidation, under the action of gaseous hydrogen fluoride and chloride at high reaction temperatures. Probably a Pd−Zn alloy is formed, with increased dispersion and stabilization of palladium metal particles avoiding deactivation.

Zhang et al. have been involved in the development of nanoscale bimetallic particles for the treatment of chlorinated organic contaminants in aqueous solutions. This group reported an efficient method of synthesizing nanoscale (1−100 nm) palladized iron particles, useful for the transformation of TCE and PCBs.[220] TCE was completely dechlorinated by palladized commercial iron powders (Pd−Fe) within 2 h, and by synthesized nanoscale Pd−Fe bimetallic particles within less than 0.25 h. Final reaction products in the headspace of nanoscale particle solutions were identified to be hydrocarbons, including ethylene, ethane, propylene, butene, butane, and pentane. Arochlor 1254 was completely dechlorinated within 17 h by the nanoscale Pd−Fe particles at ambient temperature with accumulation of biphenyl in the solution, whereas only partial reduction (<25%) was observed within the same time period with nanoscale Fe particles. In contrast, little degradation of PCBs was observed with commercial iron powders under the same experimental conditions. Nanoscale Pd−Fe particles completely and rapidly dechlorinated other substrates such as tetrachloroethene, *cis*-1,2-dichloroethene, vinyl chloride, and chlorinated benzenes.[427] The enhanced overall performance observed was rationalized in terms of an increased surface area and reactivity in which iron served primarily as electron donor and palladium as catalyst.

Experiments carried out in closed vials by Korte et al. showed that palladized iron in aqueous solution greatly accelerated the degradation of low molecular weight chlorinated aliphatic compounds such as CCl_4, $CHCl_3$, and CH_2Cl_2 to methane, and 1,1-dichloroethene, *cis*- and *trans*-1,2-dichloroethene, TCE, and tetrachloroethene to ethane.[428a,b] Apparently this bimetallic system was also effective in the reduction of halogenated aromatic compounds such as PCBs.[428c] A palladized iron column was tested under field conditions for the dechlorination of TCE in groundwater.[428d−f] The experiments demonstrated that the dechlorination reaction occurred efficiently until the surface of the Pd−Fe became fouled. Regeneration of the surface with dilute hydrochloric acid was easily accomplished, though reduced sulfur species were permanently poisoning the palladium. Removing sulfate with an anion-exchange column allowed repetitive regeneration of the Pd−Fe column for a four-week period. The high reactivity of the Pd−Fe bimetallic system was attributed to a sequence of reactions including evolution of hydrogen gas from the reduction of water by elemental iron, adsorption of hydrogen by Pd(0) with formation of powerful reducing species ($Pd\cdot H_2$, hydrogen gas intercalated into the elemental palladium lattice), and reduction of the chlorinated organic compound adsorbed on the bimetallic Pd−Fe surface.[428g]

Catalytic dechlorination of all three isomeric chlorophenols was accomplished by Pd−Fe powder in water at 28 °C.[429] The reduction product was in all cases phenol, a complete dechlorination being achieved within 5 h. Higher dechlorination rates were found with increasing bulk loading of palladium due to the increase of both the surface loading of palladium and the total surface area.

Sakata et al. developed a modified carbothermal reduction method using ion-exchange resins for the preparation of a highly stable and active Pd−Fe carbon composite (Pd−Fe/C).[430] Hydrodechlorination of chlorobenzene over this catalyst yielded benzene (90% conversion at 150 °C) as the only organic product. A substantial increase in activity was observed for the catalyst Pd−Fe/C in comparison with Pd/C and Fe/C, the two latter showing low and no activity, respectively. Scanning electron microscopy (SEM) images revealed that most of the palladium was present on the surface whereas the majority of iron was dispersed inside the catalyst particle.

Microwave heating during the preparation of alumina- and magnesia-supported palladium−iron bimetallic catalysts ($Pd-Fe/Al_2O_3$ and Pd−Fe/MgO, respectively) was reported to have an important influence on their hydrodechlorination activity.[431] More than 98% selectivity toward benzene was obtained in the hydrodechlorination of chlorobenzene using molecular hydrogen in the temperature range 140−200 °C at atmospheric pressure, the conversion being much superior in comparison with that with catalysts prepared by conventional heating. Changes in particle size, formation of palladium ions, and less susceptibility to alloy formation were the arguments used to explain the high activity of these MW-irradiated catalysts.

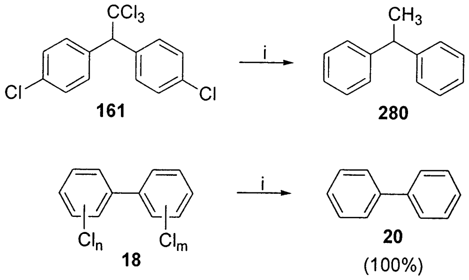
Simagina et al. studied the liquid-phase hydrodechlorination of polyaromatic compounds in the presence of the bimetallic catalyst Pd–Ni/C. Chlorobenzene, 1,2,4-trichlorobenzene, hexachlorobenzene, and polychlorinated biphenyls were efficiently dechlorinated with hydrogen in an ethanol-containing solution at 20–70 °C and 1–50 atm.[432a] The reaction rate of hexachlorobenzene hydrodechlorination was increased when the reaction was carried out with Pd–Ni/C or Pd–Cu/C in a two-phase system composed of aqueous KOH, an organic solvent (2-propanol–toluene), and alkylammonium salts as phase-transfer agents. In this medium, 98% dechlorination of hexachlorobenzene to benzene was achieved in 1.5 h at 50 °C under 1 atm of hydrogen.[432b,c] In addition to these substrates, the degree of dechlorination of the dielectric liquid Sovtol 10 (74% polychlorobiphenyls and 26% 1,2,4-trichlorobenzene) was also reported at 50–60 °C and 20 or 50 atm.[432d]

Karpinski et al. prepared a series of alumina-supported palladium–rhenium catalysts (Pd–Re/Al_2O_3) which were tested in the hydrodechlorination of CCl_2F_2 and CH_2Cl_2 using hydrogen under atmospheric pressure at 140–180 °C.[433a,b] Rhenium alone appeared to be inactive in this reaction, while addition of rhenium to Pd/Al_2O_3 introduced important changes in the catalytic behavior. As regards selectivity, an increase toward methane was observed when compared to monometallic palladium, selectivity toward CH_2F_2 changing only slightly with the bimetallic composition. Improved hydrodechlorination of CCl_2F_2 to CH_2F_2 (86% selectivity) was obtained by addition of gold to Pd/MgF_2[433c,d] and to Pd/C.[433e] The moderate selectivity exhibited by monometallic Pd/SiO_2 (~40%) in this latter transformation was also significantly improved (up to ~90%) by addition of gold. Proper Pd–Au alloying and good mixing of Pd–Au/SiO_2 catalysts were shown to be essential to obtain such remarkable selectivity; otherwise a behavior more similar to that of Pd/SiO_2 would produce substantial amounts of methane.[433f]

Rao et al. developed a wide series of carbon-supported gold-containing noble metal catalysts, among which Pd–Au (60:40)/C showed, in general, a high selectivity in the hydrodehalogenation of fluorohalocarbons and hydrofluorohalocarbons.[434]

It is generally accepted that, by removing chlorine from DDT, the hydrocarbon backbone that results is far less toxic. Cheng et al. recently reported a simple and rapid method to accomplish the complete dechlorination of DDT (**161**) in acetone–water based on the use of a magnesium–palladium bimetallic system (Scheme 102).[435a] The reaction was very fast and took place under mild reaction conditions, requiring only 0.25 g of magnesium and 0.3% palladium to drive the dechlorination of 100 μg of DDT (50 ppm in 2 mL), giving 1,1-diphenylethane (**280**) as the major product. This system was also very effective in the dechlorination of PCBs **18** (Arochlor 1221) in 2-propanol–water to produce biphenyl (**20**) in 100% yield.[435b] The main advantage of using palladized magnesium instead of iron or palladized iron is that dechlorination by Pd–Mg takes place in the presence of oxygen, no surface pretreatment being required. Moreover, the preparation of Pd–Mg was found to be much simpler and faster than that of the Pd–Fe system.

Scheme 102[a]



[a] Reagents and conditions: i, Mg–Pd, acetone–water, rt, 10 min.

We have already described the PVP-anchored monometallic or bimetallic palladium-based homogeneous catalysts introduced by Liao et al.[347] and extended by others,[348,349] which showed a synergistic effect in dehalogenation reactions. Ouyang et al. prepared a series of new dually supported bimetallic catalysts (PVP–$PdCl_2$–$SnCl_2$/Mont K10) by immobilization of PVP–$PdCl_2$–$SnCl_2$ using montmorillonite K10 as carrier.[436a,b] These catalysts showed good catalytic activity for the hydrogen-transfer dehalogenation of aryl halides, with selectivity for dechlorination and debromination. Reactions were performed in aqueous systems in the presence of a small amount of PEG(400) as phase-transfer catalyst and sodium formate as hydrogen source. The highest activity and stability were reached with a 0.19% palladium loading and a 8:1 Pd:Sn molar ratio. A higher catalytic activity and selectivity of PVP–$PdCl_2$–$SnCl_2$/Mont K10 were observed in comparison with those of the monosupported metallic or bimetallic catalysts, or with those of the dually supported monometallic catalysts. In addition, the catalyst can be easily separated and reused. The silica–polyglycol-supported polymer-anchored bimetallic palladium-based catalyst PVP–$PdCl_2$–$CuCl_2$/SiO_2–PEG(600) was also prepared, in this case by reaction of silica gel functionalized by PEG(600) (as a carrier system with phase-transfer properties) with PVP-anchored $PdCl_2$ and $CuCl_2$ complexes.[436c] With a Pd:Cu molar ratio of 2:1, the catalyst showed good activity for the dechlorination of aromatic chlorides in aqueous basic media and with sodium formate as hydrogen donor. For instance, dechlorination of *p*-chlorotoluene was effected in only 2.5 h at 80 °C with 96.6% conversion.

Several silica-supported $PdCl_2$-containing molten salts were tested as catalysts in the hydrodechlorination of CCl_4 with hydrogen at 130 °C.[437] The base catalyst $PdCl_2$–$Bu^n{}_4NCl/SiO_2$ was doped with $CoCl_2$, $CuCl_2$ or both to modify activity, product selectivity, and catalyst longevity. A mixture of products including C_1–C_5 paraffins, C_2–C_4 olefins, CH_2Cl_2, $CHCl_3$, CCl_2CCl_2, and $CHClCCl_2$ was obtained. Addition of $CoCl_2$ to the $PdCl_2$–$Bu^n{}_4NCl/SiO_2$ combination enhanced its initial CCl_4 conversion from 85% to 99.3%, increased the hydrocarbon percentage in the products, and prolonged the life of the catalyst. Although addition of $CuCl_2$ also improved the initial CCl_4 conversion (94.5%), it exhibited a stronger stabilizing effect on the catalytic activity, but shifted the reaction products toward C_1-chlorocarbons. However, the highest CCl_4 initial conversion (99.5%) and greatest longevity were achieved when both $CoCl_2$ and $CuCl_2$ were added to the base catalyst. The promotion and product distribution effects of these additives were attributed to their role as additional Lewis acidic sites for activation of CCl_4 molecules and to their interaction with the palladium-containing active centers in supported molten salt media.

Medina et al. have recently studied the catalytic behavior of several Pd−Mg−Al hydrotalcite-like materials as precursors of catalysts for the selective gas-phase hydrodechlorination of CCl_2F_2 (CFC-12) and $CHClF_2$ (HCFC-22) with hydrogen at atmospheric pressure.[438] The reaction with CCl_2F_2 led to CH_2F_2, CH_4, and $CHClF_2$, which represented more than 99% of the products. For $CHClF_2$ the main products were CH_2F_2, CHF_3, and CH_4. The increase of the palladium content in the catalysts caused an increase both in the conversion and in the selectivity toward CH_2F_2 for both substrates. High hydrogen:substrate ratios also favored the obtention of CH_2F_2, whereas a decrease in the H_2:$CHClF_2$ ratio increased the selectivity toward CHF_3.

A multimetallic catalyst containing 10% Pd, 1% Os, and 0.5% Zr on activated charcoal was prepared by treating the activated charcoal with concentrated hydrochloric acid at 80 °C for 4 h, adding the required amounts of $PdCl_2$, $OsCl_3$, and $ZrOCl_2$ in 20% HCl, and drying the slurry at 120 °C for 10 h. This catalyst was used for the selective hydrodechlorination of CF_2Cl_2 to CH_2F_2.[439]

G. Group VIIIB. Third Triad: Os, Ir, Pt

1. Osmium and Iridium

The catalytic activity of the complexes $OsHCl(CO)(Pr^i{}_3P)_2$, $OsH_2Cl_2(Pr^i{}_3P)_2$, $IrH_2Cl(Pr^i{}_3P)_2$, $IrCl(Ph_3P)_3$, and $IrH_2(SiEt_3)(COD)(Cy_3P)$ was studied in the simultaneous dehalogenation of 1,2,4-trichlorobenzene and the chlorination of triethylsilane.[312] In general, these osmium and iridium derivatives underwent deactivation, ruthenium and rhodium derivatives being more effective (see section F).

The hydrogenolysis of CCl_2F_2 over iridium on activated carbon was carried out on a micro flow reactor in a temperature range of 177−267 °C at 0.4 MPa of hydrogen pressure and showed a high selectivity for $CHClF_2$, probably due to strong chlorine adsorption.[371a−d] The results were consistent with a reaction mechanism involving difluorocarbene as the key intermediate. This Ir/C catalyst also allowed the selective hydrodechlorination of CCl_3F to $CHCl_2F$.[371d] The behavior observed was compared with the one exhibited by other supported metals (see section F).

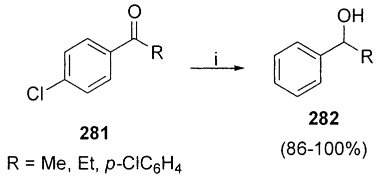
2. Platinum

Platinum as well as palladium compounds play an important role in catalysis, these two metals showing some similar catalytic properties in general heterogeneous catalysis.[440] In particular, heterogeneous catalysis using platinum metal on different supports is the most utilized methodology in platinum-catalyzed hydrodehalogenation reactions and therefore the main topic of this section. Nonetheless, an example was reported in which the three vinyl halides (Cl, Br, I) were reduced to ethylene by the system Pt(II)−NaI−$HClO_4$−H_2O.[441] Reactions were performed at 80 °C with K_2PtCl_4, the reactivity observed following the order RI ≥ RBr ≫ RCl. The oxidative addition of vinyl halides to Pt(II) was concluded to be the limiting stage of the reaction, involving the formation of an RX-π-complex and its transformation into a σ-vinyl complex accompanied by carbon−halogen bond cleavage.

Pt/C catalysts, under certain conditions, were shown to be superior in activity and selectivity to other carbon-supported metal catalysts, especially in the hydrodechlorination of some polychlorinated solvents and CFCs. For instance, a Pt/C catalyst was used in the gas-phase conversion of 1,2,3-trichloropropane (a byproduct of epichlorohydrin production) to propylene with hydrogen.[442] Among a series of eight catalysts tested, Pt/C (but also Pt/Al_2O_3) was found to yield the highest conversion for the hydrodechlorination of CH_2Cl_2, $CHCl_3$, CCl_4, 1,1,1-trichloroethane, TCE, and tetrachloroethylene. All experiments were carried out in discontinuous microreactors at 50 bar of hydrogen and at 300 °C.[443] As regards CFCs as substrates, a higher conversion of CF_3CCl_3 (CFC-113a) to CF_3CHCl_2 (up to 95%) was observed over a Pt/C catalyst in comparison with a Pd/C catalyst. The activity of the catalyst was dependent on the properties of the active carbon support and reaction temperature, the maximum conversion and yield being reached at 120 °C.[444]

We have already described the hydrodehalogenation of halogenated aryl ketones under multiphase conditions in the presence of a palladium on carbon catalyst (Scheme 96).[373e−g] Under the same reaction conditions (1 atm of H_2, isooctane, 50% KOH, Aliquat 336, and 50 °C) but using a Pt/C catalyst,[373f] several different chlorinated aryl ketones **281** were transformed into their corresponding dechlorinated benzylic alcohols **282** (Scheme 103).[445a] The presence of the phase-transfer agent Aliquat 336 was shown to be essential; otherwise, a wide range of products were obtained, including those derived from the complete reduction of both the aromatic ring and carbonyl group. When *p*-chlorobenzylic alcohols were used as substrates, the corresponding dechlorinated benzylic alcohols were obtained, albeit longer reaction times were required. By tuning the alkalinity of the aque-

Scheme 103[a]



[a] Reagents and conditions: i, H_2 (1 atm), 5% Pt/C, isooctane, 50% KOH, Aliquat 336, 50 °C, 0.25−3 h.

ous phase, it was possible to drive the course of the dechlorination of aryl ketones **281** to form the dehalogenated ketone (at low base concentrations) or the dehalogenated alcohol (at higher base concentrations).[445b] The polar phase-transfer agent film formed on the Pt/C catalyst seemed to provide a reaction microenvironment for the substrate, with functional-group-specific catalytic sites. More recently, Pt/C catalysts under multiphase conditions were successfully used in a catalytic detoxification methodology for the hydrodechlorination of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans, yielding mixtures in which the concentration of contaminants were lower than the experimentally detectable limit.[373h,i]

Hydrogenolysis of neopentyl iodide was accomplished on platinum dispersed on a magnesium oxide support, the main product at 75 °C being neopentane (>96%).[254] 2-Methylbutane and 2-methylbutenes were obtained as byproducts only at higher temperature (150° C). A π-complex-based mechanism was suggested to be involved in the activation of the carbon−iodine bond and in the evident 1,2-methyl shift observed at 150 °C.

Supported platinum catalysts were reported to be effective in the transformation of CCl_4 to $CHCl_3$ in either the liquid or gas phase (typically under pressure).[446] In particular, Lee et al. carried out a detailed study on the selective hydrodechlorination of CCl_4 to $CHCl_3$ over differently supported platinum catalysts.[447a] Among the different supports tested, Pt/MgO[447b] and Pt/Al_2O_3[447c,d] appeared to be the best catalysts for that transformation. Pt/MgO, 140 °C, and a $H_2:CCl_4$ molar ratio of 9 were found to be the optimum reaction conditions for obtaining stable and high conversions of CCl_4 (>90%). The excellent activity maintenance of Pt/MgO was believed to be due to the basic property of the support, which retards coking. The active phase of this catalyst was proposed to be platinum particles with most of their surface converted to Pt(II)−Cl moieties.[447b] With 1% Pt/Al_2O_3 the platinum precursor chosen was very important to obtain good conversion and selectivity. Thus, the Pt(II) precursors $Pt(NH_3)_4Cl_2$, $Pt(NH_3)_4(NO_2)_2$, and $Pt(NH_3)_4(NO_3)_2$ yielded catalysts with conversions close to 100% and a chloroform selectivity above 78% at 120 °C.[447c]

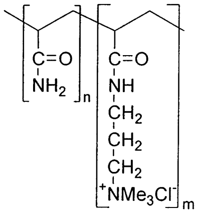
Commercially available 0.3% Pt/Al_2O_3 pellet catalysts were rapidly deactivated during the hydrodechlorination of CCl_4 to $CHCl_3$ at 90 °C and 1 atm of H_2, the conversion dropping from 90% to 2% within 1 h. However, treatment of the catalyst with a solution of ammonium chloride showed an excellent performance for over 2000 h without deactivation in this transformation.[448a,b] This remarkable behavior was attributed to an increase in the platinum particle size and its crucial role in preventing hydrogen chloride poisoning. An improved durability of this catalyst was also observed when it was treated with moist hydrogen at 500 °C for 2 h, followed by cooling to 90 °C for CCl_4 dechlorination, a 70% selectivity toward $CHCl_3$ being obtained at 90% CCl_4 conversion.[448c]

The reaction of CCl_2F_2 with hydrogen was studied on a series of $Pt/\gamma\text{-}Al_2O_3$ catalysts containing 0.5%, 2%, and 5% platinum at a temperature of 300 °C and other temperatures. The distribution of products and the extent of conversion were found to be very dependent both on the metal coverage and on the temperature.[449] Chloroethyl ethyl sulfide is a simulant of the chemical warfare agent mustard gas, which was subjected to hydrodesulfurization and hydrodechlorination by catalytic hydrogenation with 4% Pt/Al_2O_3 in a fixed bed microreactor.[450] This catalyst proved to be active and stable for 20 h at 250 °C, hydrocarbons, hydrogen sulfide, and hydrogen chloride being the reaction products.

The deactivation of Al_2O_3 and Pt/Al_2O_3 catalysts in the hydrodechlorination of 1,1,1-trichloroethane, 1,1-dichloroethylene, and 1,1-dichloroethane was studied in microreactor systems with hydrogen at atmospheric pressure over a temperature range of 150−350 °C.[451] Only the platinum-containing catalysts were able to remove all chlorine atoms from the chlorocarbons, whereas there was no reaction for dichloroethylene on Al_2O_3. Much larger quantities of coke were formed on $Pt/\eta\delta\text{-}Al_2O_3$ than on $\eta\delta\text{-}Al_2O_3$, the apparent stability of the $Pt/\eta\delta\text{-}Al_2O_3$ catalysts increasing with increasing platinum concentration. It seemed that HCl did not cause deactivation, partial or total regeneration of the catalysts being accomplished by heating in flowing He at 500 °C.

Platinum on Vycor porous glass rods was used in the smooth hydrogenation of CCl_4 at 90 °C.[389] High conversion (92%) and a 84% selectivity toward $CHCl_3$ were observed after 20 h, the general behavior of the catalyst being better than that of Pd/C. The deposition of platinum on this support seemed to favor the formation of nanoparticles of appropriate dimensions. Pt/C and Pt/Al_2O_3 were the catalysts of choice to transform $CHCl_3$ into CH_4 (90% conversion at 240 °C), whereas 72% conversion was reported for the hydrodechlorination of CH_2Cl_2 to CH_4 at 240 °C on Pt/Al_2O_3. Finally, dehalogenation of chlorobenzene at 140 °C yielded 100% cyclohexane over any of the catalysts Pt/Al_2O_3, Pt/C, Pt/Vycor, and Pt/AlF_3.

Polymer-supported platinum metal catalysts can exhibit a high selectivity, allowing the obtention of products which are not accessible with other metal catalysts.[452] Baumgarten et al. prepared a new platinum catalyst based on poly{acrylamide-*co*-[3-(acryloylamino)propyltrimethylammonium chloride]} (**283**),[453a,b] for the gas-phase hydrodechlorination of aromatic compounds.[453c] The stability of the catalyst was excellent within the experimental temperature range of 80−180 °C. Thus, the conversion of *o*-chloronitrobenzene yielded chloroaniline and aniline



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with selectivities depending on the temperature (80 and 180 °C, respectively). *o*-2-Chlorophenol was mainly reduced to cyclohexanone, while the analogous palladium catalyst led to phenol in 60% yield. The behavior exhibited by these catalysts was rationalized by an electron transfer from the nitrogen centers of the carrier to the catalytic active metal, which alters the adsorption properties of the platinum particles.

The platinum catalysts Pt/H−BEA zeolite and Pt/Al_2O_3 showed a high activity in the gas-phase hydrodechlorination of chlorobenzene. Acid-catalyzed oligomerization and coke formation provoked deactivation of Pt/H−BEA, an improved stability being observed by replacement of Brønsted acid sites by sodium ions.[454] The influence of the addition of a second metal (V, Mo, or W) on the activity and selectivity of Pt/Al_2O_3 in the above reaction was studied by Rao et al.[455] The monometallic catalyst showed a linear decrease in activity with time, whereas the bimetallic catalysts were found to be resistant to deactivation. Concerning the selectivity of the process, Pt−V/Al_2O_3 drove the reaction to cyclohexane, Pt−Mo/Al_2O_3 and Pt−W/Al_2O_3 improving the selectivity for benzene formation. The activity and resistance to poisoning of a 0.5% Pt/Al_2O_3 catalyst in the hydrodechlorination of tetrachloroethylene were also improved by addition of vanadium.[456] Experiments were carried out at 350 °C, a catalyst with 0.12% V and reduced at 500 °C giving the best performance.

Pt−Cu/C-catalyzed hydrodechlorination was used in different processes for converting chlorinated alkenes to useful, less chlorinated alkenes.[457] Thus, hydrodechlorination of tetrachloroethylene to trichloroethylene at 210 °C in the presence of a catalyst containing 0.1% Pt, 10% Cu, and 0.14 P, on an elemental basis on a carbon support, proceeded with a catalyst productivity of 411 kg/(m^3 h), much superior to that found by using Rh instead of Pt. The platinum-to-copper ratio in Pt−Cu/C catalysts was found to affect the activity and selectivity in the hydrodechorination of 1,2-dichloroethane in a hydrogen-containing atmosphere.[458] Thus, for monometallic Pt catalysts or those with a Cu:Pt ratio ≤ 1, ethane and chloroethane were practically the only compounds formed. On the other hand, increasing the copper content increased the selectivity toward ethylene (>90% for catalysts with Cu:Pt $\geq$ 1), monometallic Cu/C producing only ethylene.

To understand hydrodechlorination processes on platinum surfaces, Cassuto et al. studied both the multilayer and monolayer adsorption of a series of unsaturated chlorinated molecules (tetrachloroethene, TCE, 1,1-dichloroethene, and *cis*- and *trans*-dichloroethene) on Pt(111) and Pt(110).[459] The process seemed to occur nondissociatively at −178 °C, with the molecules only weakly bonded to the surface in the monolayer range at this temperature.

H. Group IB: Cu, Ag

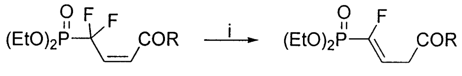
1. Copper

Copper under different forms (elemental metal, metal oxide, and metal halide) was utilized as a catalyst in the vapor-phase hydrodehalogenation of $CF_3CCl_2CF_3$ with hydrogen at elevated temperatures, giving rise to pentafluoropropenes $CF_3CX{=}CF_2$ (X = H, Cl).[460]

Apparently, a new reaction was discovered by Buijs consisting in the catalytic reduction of polyhalogenated aromatic hydrocarbons by copper(I) benzoate under Dow-Phenol conditions in the absence of air.[461] This homogeneous reaction, with carbon dioxide production, was applied to 1,3,5-tribromobenzene, 1-bromo-2-chlorobenzene, hexachlorobenzene, bis(*p*-bromophenyl) ether, and 1,3,5-trichlorobenzene, the two latter leading to a somewhat lower CO_2 production. A distribution of products with different dehalogenation degrees together with starting material was obtained, the limit of the number of carbon−halogen bonds that can be reduced per copper ion being close to one. The presence of dimeric copper(I) and copper(II) benzoates was suggested to be essential in the control of both the geometry and electronics of the reaction, two SET steps from the two Cu(I) atoms in the dimer being proposed as a part of the mechanism.

In an attempt to introduce a methyl group on the γ-difluoro-α,β-enoate **284**, by conjugate addition of an organocopper reagent, the corresponding (*E*)-γ-fluoro-β,γ-enoate **285** was the main reaction product obtained (Scheme 104).[462] The reactions were performed with either MeCu(CN)Li or $Me_2Cu(CN)Li_2$ in the presence of LiCl and/or $AlCl_3$ at −78 °C, no alkylation being observed. This unexpected organocopper-mediated reduction can be considered a formal hydrodefluorination reaction followed by isomerization of the carbon−carbon double bond and found application in the preparation of phosphopeptide mimetics.

Scheme 104[a]



284 **285**

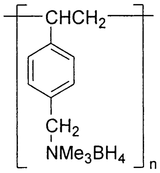
R = (2*S*)-bornane-[10,2]-sultam (92%)

[a] Reagents and conditions: i, $Me_2Cu(CN)Li_2 \cdot 2LiBr \cdot 2LiCl$, THF, −78 °C, 1.5 h.

Borohydride exchange resin (BER) (**286**) is a milder reducing agent than $NaBH_4$ widely studied by Yoon et al., which by addition of catalytic amounts of $CuSO_4$ in methanol gives a black coating of copper on BER. The BER−$CuSO_4$(cat) system was shown to be very efficient and highly chemoselective in the reduction of organic halides, above all bromides and iodides, alkyl and aryl chlorides remaining unaffected (Chart 31).[463] Selective debromination of *p*-bromochlorobenzene and deiodination of *p*-bromoiodobenzene were achieved in excellent yields (99% and 97%, respectively).

The dechlorination of hexachlorobenzene on activated municipal waste incinerator fly ash was studied in the temperature range of 150−350 °C in closed systems under nitrogen and in the presence of different additives (Cu, CuO, MgO, PbO, ZnO, H_2O, and 2-methoxyethanol).[464] Cu powder and CuO exhibited the best performance, the addition of the former resulting in 76% dechlorination at 260 °C to

Chart 31. Hydrodehalogenation of Organic Halides with BER (286)−$CuSO_4$(cat) in MeOH at rt for 1 h



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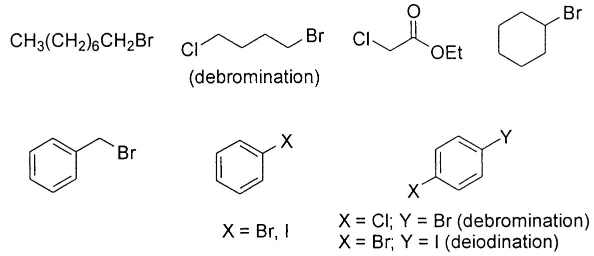


yield a 1:1 mixture of dichlorobenzenes and chlorobenzene. A catalytic process with participation of Cu(0) and/or Cu(I) sites was suggested to take place. The adsorption, activation energies for carbon−halogen bond scission, and identification of intermediates and products in the chemical reaction of organic halides (above all chlorinated ethanes, propanes, and ethenes) on copper surfaces were studied in some detail by Raval et al.[465] among others.[466]

2. Silver

As mentioned before, Gellman et al. studied in detail the kinetics and transition state for dehalogenation reactions on palladium surfaces.[420] This work was extended to silver surfaces.[420c,d,467] In particular, the kinetics of carbon−iodine bond cleavage on the Ag(111) surface was measured in a set of 10 alkyl and fluoroalkyl iodides. The estimated barrier for carbon−iodine cleavage proved to be sensitive to the nature of the alkyl or fluoroalkyl substituent groups bonded to the α-carbon atom, the reaction constants being quite low. Although these results suggested that the transition state for the carbon−iodine bond cleavage would be slightly anionic with respect to the adsorbed iodide, it was concluded that the transition state is fairly homolytic in the sense that it occurs early in the reaction coordinate and it is more like the initial-state iodide.

Subcolloidal (<0.1 μm) iron−silver (1% Ag) particles were synthesized for the transformation of chlorinated benzenes in aqueous solution.[468] Hexachlorobenzene was dechlorinated within 24 h at a metal loading of 25 g/L, the principal degradation products including 1,2,4,5-tetrachlorobenzene, 1,2,4-trichlorobenzene, and 1,4-dichlorobenzene. Continuous dechlorination was observed during a 57 d experiment. The rate of dechlorination was positively correlated to the silver loading of the bimetallic particles, which in addition were also effective in the degradation of penta- and tetrachlorobenzenes. The Fe−Ag particles could become a cost-effective alternative to the previously reported Pd−Fe particles (see section F).

Heinrichs et al. prepared a series of palladium−silver sol−gel catalysts (Pd−Ag/SiO_2), palladium alloy particles having diameters of about 2−3 nm and being dispersed inside the silica particles.[469] These low-density xerogels were utilized in the catalytic hydrodechlorination of 1,2-dichloroethane at a temperature range of 200−300 °C and 0.3 MPa of H_2. A very high selectivity to ethane ($>95\%$) was observed at 200 °C for a 2:1 Pd:Ag ratio, whereas increasing both the amount of silver and temperature clearly favored selectivity to ethylene. It was suggested that the active sites are silver atoms present at the surface of the Pd−Ag alloy particles. Silver is more active than palladium in carbon−chlorine bond dissociation, but chlorine does not desorb from silver. So, palladium probably promotes hydrogen dissociation and migration of hydrogen atoms to silver, regenerating chlorinated silver, but also promotes hydrogenation of ethylene to ethane. It was also suggested that chlorine atoms induce positively charged surface silver atoms, which are the effective active sites.

A very efficient dechlorination methodology of PCBs (Arochlor 1242 and 1248) was reported by Marshall et al., using heated columns with the bimetallic mixtures Ag−Fe and Ag−Ni in a continuous process in the presence of $scCO_2$.[228] $scCO_2$ showed a good substrate solubility, allowing its transfer through the reactor with enhanced diffusion rates. The bimetallic mixtures further improved both the dechlorination yield and the repeatability of the reaction in comparison with some monometallic zerovalent metals (Cu, Fe, Ni, and Zn). Addition of DME to the solvent (acetic anhydride) increased the yield by 9% and 14% for the Ag−Fe and Ag−Ni mixtures, respectively, dechlorination of substrates at 400 °C and 4500 psi being practically quantitative. Under similar conditions, the zerovalent Ag−Fe bimetallic mixture achieved practically quantitative dechlorination of pentachlorophenol, phenol, methylated phenols, and methylated benzenes being the only reaction products, no chlorinated aromatics being detected.[470]

I. Group IIB: Zn

Zinc in the zerovalent state found important applications as a reductant in hydrodehalogenation processes. Even in other types of reactions involving organic halides, and due to its reducing ability, substantial amounts of reduced compounds can be obtained as byproducts. Such is the case for the zinc Barbier reaction of benzylic halides in water reported by Bieber et al.[471] Although the presence of catalytic amounts of lead(II) or silver(I) produced more addition to carbonyl product in comparison with the uncatalyzed reaction, hydrodehalogenation of benzyl chlorides and bromides was an important side reaction occurring with yields up to 71%.

Dehalogenation of carbon tetrachloride using zerovalent zinc has attracted the attention of different research groups. For instance, elemental zinc reduced part-per-thousand levels of aqueous-phase (2-propanol−water) carbon tetrachloride to chloroform in a few hours.[214] The process kinetics was dependent on the solution pH, surface area of the elemental metal, carbon tetrachloride concentration, buffer selection, and solvent composition. The reaction rate was proportional to the surface area of the suspended metal, whereas a decrease was observed with increasing pH.

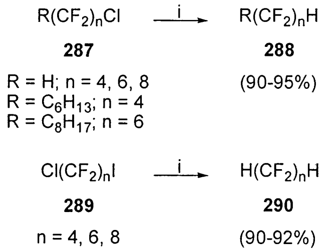
An important contribution to this field was done by Boronina et al., who demonstrated that metallic zinc is an ideal candidate for the practical destruction of carbon tetrachloride in water.[472] In a preliminary work, zinc dust was reported to cause deep sequential dechlorination of carbon tetrachloride to give methane as the main final organic product, chloroform, methylene chloride, and methyl chloride being intermediate reaction compounds.[472a] In general, superior and different behavior was observed for zinc in comparison with magnesium or tin, the most active samples being prepared by a metal vapor−solvent codeposition method (cryoparticles) or by mechanical treatment.[472a−e] Doping zinc with silver, palladium, or gold resulted in a 4−10-fold increase in the carbon tetrachloride degradation rate and conversion to methane.[472f] Surface activation was suggested to facilitate the initial and rate-determining electron-transfer step. An interesting debate emerged around the mechanisms of the compared zinc- and tin-mediated carbon tetrachloride hydrodehalogenation reactions, in terms of both reduction−oxidation potentials and solution pH, and in terms of surface reaction mechanims.[473]

Detoxification of chlorinated hydrocarbons in aqueous solution was effected by a low-energy dechlorination technique based on the use of metal particles or copper-activated metal particles (Mg, Fe, Al, and Zn).[474] Experiments were performed in a laboratory-scale fixed bed reactor in which zinc proved to be the optimum reducing agent achieving the best space−time yield. As an example, chloroform was transformed into methane with 99.4% conversion at 85 min. Lindane and 1,1,1-trichloroethane were also completely dechlorinated to benzene and ethane, respectively, chlorobenzene not undergoing reductive dechlorination. Zerovalent zinc was also applied in the stoichiometric dechlorination of octachlorodibenzo-*p*-dioxin to hexa- and pentachlorodibenzo-*p*-dioxin under basic and neutral conditions, respectively.[475]

1,1,1-Trichloroethane was found to react rapidly with zinc in an aqueous medium to form ethane and 1,1-dichloroethane.[476a] Independent experiments confirmed that 1,1-dichloroethane reacted too slowly to represent an intermediate in the formation of ethane. Other metal or bimetallic reductants (Fe, Ni−Fe, and Cu−Fe) also led to elimination products, with zinc resulting in the lowest yield of chlorinated products. Chloroacetylene and dichloroacetylene also reacted rapidly with zinc, the products being consistent with both hydrogenolysis and reduction of the carbon−carbon triple bond.[476b]

Huang et al. reported a new reduction system composed of zinc and hydrazine hydrate for the hydrodehalogenation of polyfluoroalkyl halides **287** and **289** (Scheme 105).[477] This methodology was applied to both perfluoroalkyl chlorides and iodides in DMF at 70−80 °C for 2 h to furnish the corresponding reduced products **288** and **290** in high yields. Chemoselective carbon−iodine bond cleavage was observed for $Cl(CF_2)_6I$ in the absence of hydrazine hydrate, whereas reduction of the CF_2Cl moiety was found to be faster than that of the CHI moiety in other substrates.

Scheme 105[a]

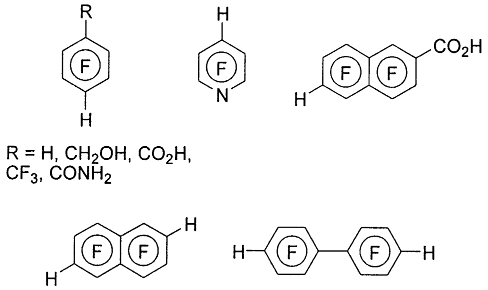


[a] Reagents and conditions: i, Zn, $N_2H_4{\cdot}H_2O$, DMF, 70−80 °C, 2 h.

Reductive defluorination of perfluoroarenes and perfluoroalkylarenes has been a subject of great interest during the past decade, metallic zinc playing a remarkable role for this process as reducing agent in different media. For instance, treatment of pentafluorobenzonitrile with Zn powder and aqueous KH_2PO_4, at 100 °C for 2 h, led to 2,3,5,6-tetrafluorobenzonitrile in 94% yield at 100% conversion.[478]

Shteingarts et al. used zinc in ammonia under mild conditions for the selective reductive defluorination of perfluoroarenes (Chart 32).[479] At the beginning of this research it was found that defluorination of pentafluorobenzoic acid with sodium in ammonia led to a complex mixture of products with low conversion. In contrast, regioselective defluorination at the *para*-position with >90% yield took place when zinc was used instead of sodium.[479a] *para*-Defluorination was also observed for 2,3,4,5-tetrafluorobenzoic acid, 2,3,4,5,6-pentafluorobenzyl alcohol, and pentafluoroaniline, heptafluoro-2-naphthoic acid being defluorinated at the 6-position and octafluoronaphthalene at the 2- and 6-positions (Chart 32).[479b] An ammonia concentration effect was observed in the hydrodefluorination of hexafluorobenzene, octafluorotoluene, octafluoronaphthalene, and decafluorobiphenyl, the presence of ammonium chloride and the addition of an organic solvent (THF or Et_2O) having a significant effect in the two latter substrates, respectively.[479c] This methodology was extended to the *para*-defluorination of pentafluorobenzamide and the chemoselective dechlorination of chloroperfluorinated arenes. A reduction mechanism involving direct electron transfer from zinc to the substrate, followed by

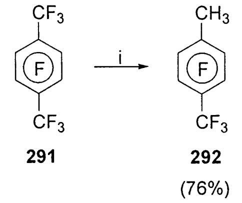
Chart 32. Products Obtained by Regioselective Defluorination of the Parent Perfluorinated Arenes with Zn and 20−30% aq NH_3 (with or without NH_4Cl or THF) at rt for 15 min to 39 h (30−99%)



fragmentation of the resulting radical anion, was suggested.[479d]

The system Zn−Cu−DMF−H_2O developed by Platonov et al. was shown to be an alternative to the previous one described, for the efficient hydrodefluorination of perfluoroarenes and perfluoroalkylarenes.[480] Thus, hydrogenolysis of heptafluoro- and hexafluoroisopropyl groups in polyfluoroaromatic compounds was described with the above system.[480a,b] Starting form C_6F_5R (R = CN, CF_3, $CF_2CF_2CF_3$) under the above conditions, the corresponding *para*-defluorinated compounds were obtained in 47−71% yield. Similar results were observed for perfluorobenzoic acid, perfluoropyridine, and perfluoro-*m*-xylene, whereas the 5-H derivative was obtained from perfluoroindan (15−70%).[480c] Selective reduction of carbon−chlorine bonds in perfluoroarenes and selective defluorination at the benzylic positions were also reported.[480d] A complete study on the transformations of perfluoroxylenes and perfluoro-*p*-cymene by the Zn−Cu−DMF−H_2O system brought out the dependence on the position and structure of the perfluoroalkyl group. Thus, reactions of perfluorinated *m*- and *o*-xylenes affected aromatic carbon−fluorine bonds, whereas side chain hydrodefluorination predominated in the case of perfluorinated *p*-dialkylbenzenes (Scheme 106).[480e] Product formation was explained by the same electron-transfer mechanism proposed by Shteingarts et al.[479]

Scheme 106[a]

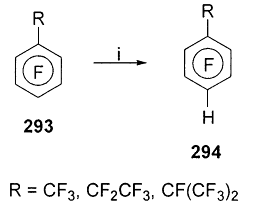


[a] Reagents and conditions: i, Zn−Cu, DMF, H_2O, 70 °C, 20 h.

More recently, it was found that polyfluoroarenes with chlorine atoms in the aromatic ring and/or at the benzylic position underwent hydrodechlorination by the action of zinc in aqueous DMF, the use of Zn−Cu and the addition of salts (NaCl, Na_2SO_4, or NH_4Cl) favoring the reductive dechlorination of the aromatic carbon−chlorine bond. In contrast, complete dechlorination of the CCl_3 moiety in trichloromethyl-substituted polyfluoroarenes was only achieved with an excess of zinc, the presence of copper providing lower yields and coupling products.[480f] Perfluoroalkylbenzenes **293** underwent regioselective *para*-defluorination with zinc and either copper or copper(II) chloride in DMF−H_2O and in the presence of either ammonium or sodium chloride (Scheme 107).[480g] However, tetradecafluoro-*tert*-butylbenzene suffered defluorination at both the *ortho*- and *para*-positions, and hexadecafluoro-4-*tert*-butyltoluene at the *ortho*-position with respect to the $C(CF_3)_3$ group.

In situ generation of hydrogen from zinc and an organic acid such as acetic, formic, citric, or tartaric acid found application in the hydrodechlorination of polyhalogenated compounds such as DDT, DDD, DDE, and hexachlorobenzene, contained in contaminated soil, with 4−8 h contact times.[481] The system Zn−HOAc in DMF was also successfully utilized in the transformation of aryl trifluoromethyl ketones into the corresponding aryl methyl ketones in good yields.[482]

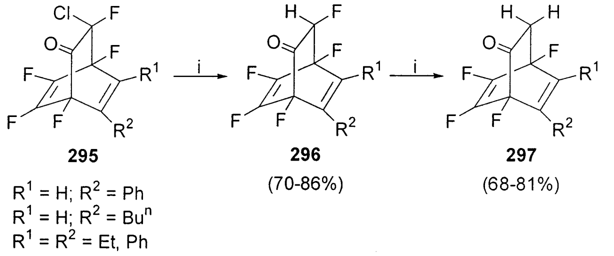
Scheme 107[a]



[a] Reagents and conditions: i, Zn−Cu (or $CuCl_2$), DMF, H_2O, NH_4Cl (or NaCl).

As an example of the dehalogenation ability of zinc in synthetic organic chemistry, Kobrina et al. described the selective reductive dehalogenation with zinc in acetic acid of 8-chloro-1,2,3,4,8-pentafluorobicyclo[2.2.2]octa-2,5-dienones **295**, bearing alkyl and aryl substituents at the carbon−carbon double bond (Scheme 108).[483] Successive hydrodechlorination and hydrodefluorination were observed at the 8-position, the resulting products **296** and **297** being subjected in a further step to aromatization with sodium hydroxide.

Scheme 108[a]



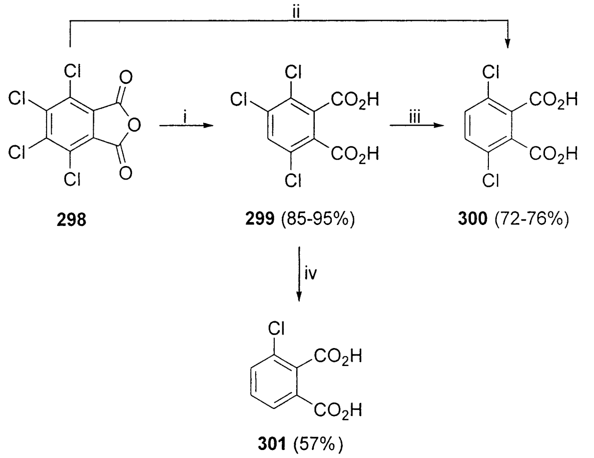
[a] Reagents and conditions: i, Zn, HOAc, reflux, 2−16 h.

O'Reilly and Fertel et al. reported the high yield and selective hydrodechlorination of 3,4,5,6-tetrachlorophthalic anhydride **298** with zinc dust in aqueous sodium hydroxide.[484a,b] The degree of dechlorination could be controlled by adjusting the temperature, amount of zinc, and reaction time (Scheme 109). Thus, by using 3 equiv of zinc with 5% NaOH at 65 °C for 3−5 h, 3,4,6-trichlorophthalic acid **299** was obtained in 85−95% yield. With longer reaction times and 10% NaOH at 105 °C, the starting material was transformed into 3,6-dichlorophthalic acid **300** in 76% yield, which alternatively could be obtained from 3,4,6-trichlorophthalic acid **299** in 72% isolated yield with 5.7 equiv of zinc and 10% NaOH at 100 °C for 3.5 h. Finally, 3-chlorophthalic acid **301** was also prepared from 3,4,6-trichlorophthalic acid **299** in 57% isolated yield with 5.7 equiv of zinc and 20% NaOH at 118 °C for long reaction periods. In a similar manner, this methodology was extended to the regioselective hydrodefluorination of tetrafluorophthalimide derivatives.[484c,d]

VII. Lanthanides and Actinides

The chemistry of lanthanide elements has undergone an important development during the last two

Scheme 109[a]

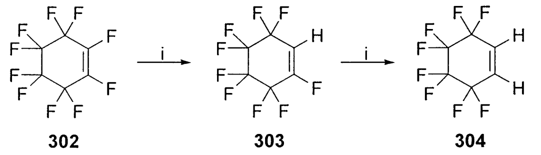


[a] Reagents and conditions: i, Zn (3 equiv), 5% NaOH, 65 °C, 3−5 h; ii, Zn (3 equiv), 10% NaOH, 105 °C; iii, Zn (5.7 equiv), 10% NaOH, 100 °C, 3.5 h; iv, Zn (5.7 equiv), 20% NaOH, 115 °C, 65 h.

decades, being considered a very useful tool from the technological, industrial, and synthetic points of view. In particular, lanthanide complexes emerged as unique reagents in some methodologies due to their unusual high reactivity and catalytic activity.[485]

In an early 1990s report, Watson et al. described the rapid defluorination of certain perfluoroolefins by divalent lanthanoid complexes of the types MCp^*_2 (M = Yb, Sm, Eu) and $YbCp'_2$ ($Cp' = \eta^5$-methylcyclopentadienyl).[486] The corresponding trivalent lanthanoid−fluoride complexes were also obtained as a result of the intermolecular fluorine abstraction. The negative reduction potentials of the metal ions [M(III)−M(II) couple], together with the formation of the very strong lanthanoid−fluoride bond, were suggested as the main driving forces for this reaction. As an example, perfluorocyclohexene (**302**) was hydrodefluorinated at the olefinic carbon atom to give 2,3,3,4,4,5,5,6,6-nonafluorocyclohexene (**303**) as the primary initial product, which suffered further transformation into 3,3,4,4,5,5,6,6-octafluorocyclohexene (**304**) and pentafluorobenzene, the latter obtained by different routes (Scheme 110). Deuterium-labeling studies indicated that the hydrogen source was not the solvent but probably the cyclopentadienyl rings of the organometallic reagents.

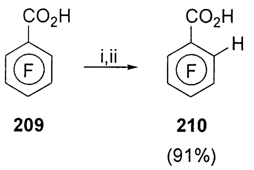
Scheme 110[a]



[a] Reagents and conditions: i, $MCp^*_2{\cdot}OEt_2$ (M = Yb, Sm, Eu) or $YbCp'_2{\cdot}THF$.

Regiospecific defluorination of pentafluorobenzoic acid (**209**) was achieved with the ytterbium(II) complex $YbCp_2(dme)$[487a] in THF at room temperature, giving rise to 2,3,4,5-tetrafluorobenzoic acid (**210**) (Scheme 111).[487b] Conversion was near quantitative in the presence of activated magnesium as coreductant, catalytic turnover in ytterbium being evidenced by the addition of a cyclopentadiene source (CpH or CpTl). This reducing system was also applied to the defluorination of *o*-fluorobenzoic acid as well as to the monodefluorination or complete defluorination of 2,6-difluorobenzoic acid. Intramolecular electron transfer and fluoride abstraction from cyclopentadienylytterbium(II) pentafluorobenzoate, through a cyclic six-membered transition state, was suggested as a plausible rationale to account for the regiochemistry observed.

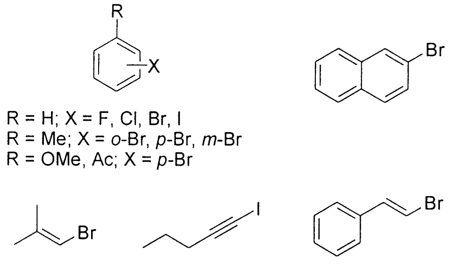
Scheme 111[a]



[a] Reagents and conditions: i, $YbCp_2(dme)$, MgI_2, THF, rt, 0.25 h; ii, acidic hydrolysis.

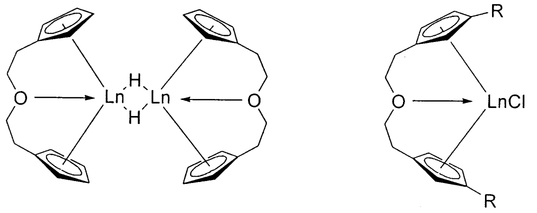
Qian et al. studied a wide range of organolanthanide complexes in combination with sodium hydride as effective systems for the reductive dehalogenation of aryl and vinyl halides.[488] Thus, reductive dehalogenation of *p*-bromotoluene with sodium hydride in THF using Cp_3La as catalyst furnished toluene in 100% yield. In a similar way, *p*-iodochlorobenzene and *β*-bromostyrene gave chlorobenzene and styrene, respectively (97−100%). Alternatively, Cp_3Y and Cp_2YCl could be used instead of Cp_3La.[488a] In a more detailed publication, the activities of several tricyclopentadienyllanthanide complexes for the above reaction were found to follow the decreasing order $Cp_3La > Cp_3Sm > Cp_3Gd > Cp_3Y > Cp_3Lu$, THF being the solvent of choice.[488b] A wide range of aryl and vinyl halides, including fluorides, chlorides, bromides, and iodides, were successfully dehalogenated with Cp_3La under mild reaction conditions (45 or 65 °C), most yields being >95% (Chart 33). However, alkylated products were obtained when alkyl halides were used as substrates. A *μ*-hydride complex was proposed as the active reducing species.

Chart 33. Reductive Dehalogenation of Organic Halides with Cp_3La−NaH in THF at 65 °C (or 45 °C) for 1−48 h (44−100%)



Dimeric organolanthanide hydrides $[O(CH_2CH_2C_5H_4)_2LnH]_2$ (**305**) (Ln = Gd, Er, Yb, Lu, Y), obtained by reaction of $[O(CH_2CH_2C_5H_4)_2]LnCl$ with NaH, were utilized in the hydrodehalogenation of both aryl and alkyl bromides and iodides in THF at 65 °C, very high yielding processes being observed with the more active system **305**−NaH, which in addition could function catalytically.[488c] Similar catalytic effectiveness for this purpose was exhibited by the *ansa*-metallocene chloride systems $O(CH_2CH_2C_5H_3R)_2LnCl$

Chart 34. Lanthanide Complexes Used in Combination with NaH for the Reductive Dehalogenation of Organic Halides



305
Ln = Gd, Er, Yb, Lu, Y

306
Ln = Sm, Nd, Yb, Y
R = Bu^t, $SiMe_3$

(**306**)−NaH (Ln = Y, Sm, Nd, Yb; R = Bu^t, $SiMe_3$) (Chart 34).[488d] Two further types of lanthanide complexes, Cp_2LnCl and $Ln(OPr^i)_3$, were investigated as catalysts in the NaH reduction of organic halides.[488e] Within the former group of complexes, the Cp_2YCl−NaH system showed a high reactivity, catalyzing the carbon−halogen bond cleavage of both aryl and activated alkyl halides, an organoyttrium hydride being suggested as the reactive species. Within the second group, $Sm(OPr^i)_3$ was the most active catalyst (higher than Cp_2YCl), an aggregate probably being involved in the proposed mechanism.

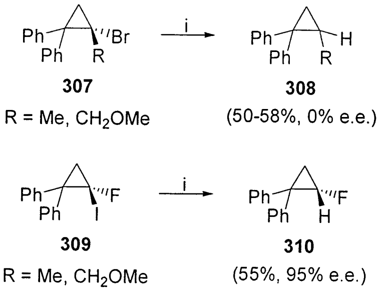
Sodium hydride of nanometric size[48a] developed by Liao et al. exhibited a high reactivity for the reductive dehalogenation of aryl halides in the presence of catalytic amounts of lanthanide chloride or a mixture of lanthanide chloride and a transition-metal chloride.[489] The catalytic activity of the lanthanide chloride was found to decrease as the atomic number of the rare-earth element increased: $LaCl_3 > NdCl_3 > SmCl_3 > DyCl_3 > YbCl_3$. Reactions were performed in THF at 60 °C for 4 h, conditions under which $LaCl_3$–NaH led to 100% chlorobenzene conversion. The remarkable behavior of these catalysts was demonstrated in their application to defluorination of fluorobenzene, though conversions were moderate (35−41%). Different catalytic activities in $SmCl_3$ were observed by substitution of chlorine atoms by Cp groups [Cp_nSmCl_{3-n} ($n = 1-3$)], the best results being obtained for the complex Cp_2SmCl. A synergistic effect by combination of the lanthanide chloride with a transition-metal chloride ($NiCl_2$, $CoCl_2$, VCl_3, $FeCl_3$) increased the rate of the reaction in the order $YbCl_3 > SmCl_3 > LaCl_3$, just the opposite of that when the lanthanide chloride was used alone as catalyst.

An enhanced reducing ability of lanthanide halides was achieved by irradiation with near-UV light. Upon irradiation with light of wavelength over 300 nm, ytterbium(II) iodide exhibited a reducing power similar to that of samarium(II) iodide in THF (see below). This photoinduced reduction system was utilized in the reductive hydrodebromination of primary, secondary, tertiary, and aromatic bromides in THF at 30 °C.[490] A catalytic version of this reaction was also reported with catalytic amounts of YbI_2 and an excess of aluminum as coreductant.

To the best of our knowledge, lanthanides in the zerovalent state have been scarcely used in hydrodehalogenation reactions, their main tendency being to promote dehalogenation in *vic*-dihalides. In fact, the fast and quantitative transformation of dimethyl *dl*-2,3-dibromosuccinate into dimethyl succinate by Sm was attributed to overreduction of the intermediate product dimethyl fumarate.[491] On the other hand, during the recent decades samarium(II) iodide has demonstrated to be a unique reagent essential for a multitude of organic transformations.[492] In particular, as a one-electron reducing agent it has been applied to the chemoselective reduction of a large variety of functional groups, and also in hydrodehalogenation reactions.

Thus, Walborsky et al. studied the reduction of enantiomerically pure cyclopropyl halides **307** with samarium(II) iodide in THF−HMPA at room temperature to give the corresponding hydrocarbons **308**, almost racemic (Scheme 112).[493] In contrast, when derivative **309** was subjected to the same process, **310** was obtained with overall retention of configuration (95% ee), samarium(II) iodide acting as an excellent radical trap toward the corresponding intermediate radical species. Evidence for a samarium(III) intermediate in the reaction was also presented.

Scheme 112[a]



307
R = Me, CH_2OMe

308
(50-58%, 0% e.e.)

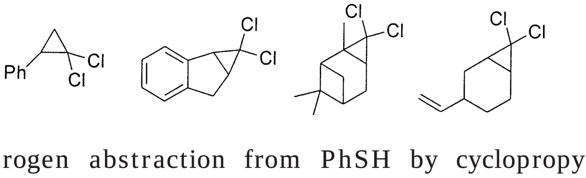
309
R = Me, CH_2OMe

310
(55%, 95% e.e.)

[a] Reagents and conditions: i, SmI_2, THF, HMPA, rt, 2 h.

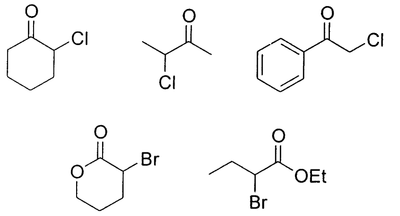
In the absence of HMPA but upon irradiation with visible light, *gem*-dichlorocyclopropanes could be completely hydrodechlorinated with SmI_2 and benzenethiol to the corresponding cyclopropanes in good yields (Chart 35).[494] The reaction probably involves hydrogen abstraction from PhSH by cyclopropyl radicals formed in situ through photoinduced one-electron transfer from SmI_2. In the absence of a hydrogen donor, a mixture of products was obtained, cyclopropyl radicals abstracting hydrogen from the solvent (THF).

Chart 35. Complete Hydrodechlorination of *gem*-Dichlorocyclopropanes with SmI_2, PhSH, and $h\nu > 300$ nm in THF at rt (46−77%)



A samarium(II) iodide equivalent, generated from the Sm−Me_3SiCl−NaI system, was satisfactorily applied to the dehalogenation of α-halocarbonyl compounds under mild reaction conditions (−40 °C) (Chart 36).[495] Acetonitrile was the best solvent, methanol being included as proton source to protonate the resulting samarium enolate. Under these conditions, aliphatic, cyclic, and aromatic α-chloroketones, as well as an example of both α-bromolactone

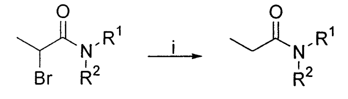
Chart 36. Reductive Dehalogenation of α-Halocarbonyl Compounds with Sm−Me_3SiCl−NaI in MeCN−MeOH at −40 °C for 0.5 h (82−99%)



and ester, were readily reduced to the corresponding ketones and esters, respectively, in very good yields. Hydrodehalogenation of aromatic α-bromoketones was also accomplished with samarium(III) iodide in THF and EtOH.[496] The method was compatible with the presence of other functional groups on the aromatic ring such as chlorine, bromine, or the nitro group.

In connection with the enantiospecific synthesis of atropisomeric amides, Simpkins et al. described the SmI_2-mediated debromination of structurally different α-bromoamides **311** under mild reaction conditions, affording the expected reduced amides **312** in moderate to good yields (Scheme 113).[497]

Scheme 113[a]



311 **312**

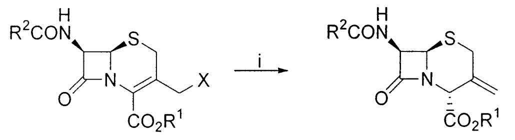
R^1 = H, Me (57-72%)

R^2 = Ph, o-$Bu^tC_6H_5$

[a] Reagents and conditions: i, SmI_2, THF, rt, 24 h.

A new approach to the synthesis of exomethylene cephams **314** based on the use of samarium(II) iodide was described by Cabri et al., which proved to be chemo-, regio-, and stereoselective (Scheme 114).[498]

Scheme 114[a]



313 **314**

R^1 = p-$MeOC_6H_4CH_2$, Ph_2CH, Me (62-85%)

R^2 = Ph, Bn, $PhOCH_2$

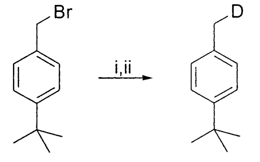
X = Cl, I

[a] Reagents and conditions: i, SmI_2, THF, H_2O, HMPA, rt, 2 h.

This methodology took advantage of the ability of samarium(II) to generate allylsamarium(III) complexes starting from the corresponding allyl halides **313**, in the presence of a suitable proton source (water showed in this case the best performance). The exomethylene cepham **314** with the natural configuration at C-4 was the only product present in the final mixture, no endomethylene cepham being detected. This reducing system, compatible with several protective groups, was practically independent of the reaction temperature.

Mischmetall is an alloy of light lanthanides (La, 33%; Ce, 50%; Nd, 12%; Pr, 4%; Sm and other lanthanides, 1%) utilized as coreductant in samarium(II) iodide-catalyzed hydrodehalogenation of alkyl halides.[499] For instance, slow addition (over 3 h) of 1-iodododecane to a THF−SmI_2−mischmetall suspension led quantitatively to a mixture of dodecane and 1-dodecene in a 2:1 ratio. When 4-*tert*-butylbenzyl bromide (**315**) was used as starting material and the reaction mixture was quenched with D_2O, 88% incorporation of deuterium into deuterated 4-*tert*-butyltoluene (**316**) was observed together with small amounts of 4,4′-di-*tert*-butyldibenzyl (Scheme 115).

Scheme 115[a]



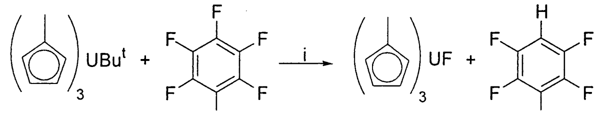
315 **316**

[a] Reagents and conditions: i, SmI_2, mischmetall, THF, 20 °C, 4 h; ii, D_2O, 1 h.

Ogawa et al. found an enhanced ability in the hydrodehalogenation of alkyl halides by combining samarium(II) iodide and samarium metal.[500] The Sm−SmI_2 system allowed the smooth reduction in 2-propanol of primary alkyl halides 1-bromo- and 1-iodododecane (rt, 45 min, 88%; rt, 4 h, 78%, respectively), secondary alkyl halide 2-bromooctane (rt, 5 h, 78%), and tertiary alkyl halide 1-bromoadamantane (rt, 15 h, 95%). However, 1-chlorododecane was hydrodechlorinated in only 30% yield at 67 °C after 20 h. The difference of reactivity between bromides and chlorides toward the Sm−SmI_2 system enabled the selective reduction of 1-bromo-6-chlorohexane to 1-chlorohexane (rt, 20 h, 68%).

Finally, to the best of our knowledge, uranium has been the only actinide element involved in the topic of this review, more specifically in the intermolecular abstraction of fluorine atoms from perfluorocarbons.[501] For instance, the complex $(MeC_5H_4)_3U(Bu^t)$ (**317**) reacted with hexafluorobenzene (**167**) in toluene solution at room temperature, giving rise to the uranium(IV) fluoride $(MeC_5H_4)_3UF$ (**318**) in quantitative yield (Scheme 116). Pentafluorobenzene (**171**) was the main organic product obtained (50%), together with $C_6F_5(Bu^t)$, isobutane, and isobutene. An increase in the yield of C_6F_5H relative to $C_6F_5(Bu^t)$ was observed with increasing reaction temperature, a radical cage mechanism being consistent with the product distribution obtained. Under the same reaction conditions, perfluorocyclohexane (C_6F_{12}) led to

Scheme 116[a]



317 **167** **318** **171**

(50%)

[a] Reagents and conditions: i, PhMe, rt, 24 h.

$C_6F_{11}H$ in 45% yield. The role of toluene as hydrogen donor was confirmed by the obtention of $C_6F_{11}D$ when the reaction was performed in toluene-d_8.

VIII. Conclusions

In this review we have highlighted how abundant and spread are halogenated compounds in the Earth nowadays, proceeding from either natural or artificial sources. There is no doubt about their irreplaceable role as secondary metabolites in living organisms, or about the multiple applications of those man-made, with the consequent benefits for mankind. In the same way, the important utilities of organic halides in synthetic organic chemistry must not be neglected. Ignorance, on one hand, and political or economical interests, on the other hand, led to the uncontrolled production of halogenated materials which through the derived wastes and emissions cause a direct or indirect deleterious effect on the environment, in many cases with irreparable consequences.

We have demonstrated throughout this review that the metal-mediated hydrodehalogenation reaction is of paramount importance as a reducing method for the appropriate treatment of these chemicals, and promises to be a reasonable solution for either their complete detoxification or their transformation into less noxious chemicals. The importance of this reaction is confirmed by the fact that this topic has attracted the attention of scientists involved in such different disciplines such as organic chemistry, inorganic chemistry, organometallic chemistry, chemical engineering, catalysis, surface science, or earth and environmental sciences. From the alkaline metals to the lanthanides, we can find a wide array of reagents which under different forms and conditions can be adjusted to the hydrodehalogenation of practically any type of substrate, in many cases with remarkable results.

Concerning alkali and alkaline-earth metals, the most important hydrodehalogenation methodologies involve the use of active zerovalent metals. Reactions take place through SET processes in the presence of a proton source, or by direct synthesis of the corresponding organometallic derivative followed by protonation. Alternatively, the intermediate organometallic species can be generated by halogen−metal exchange with lithium amides, alkyllithium, or Grignard reagents. One main advantage of this methodology is the easy preparation of labeled products by halogen−deuterium (or tritium) exchange using convenient labeled reagents or solvents. However, its application is practically restricted to a laboratory scale due to the high reactivity, moisture sensitivity, and special handling of these reducing agents.

The reactivity of group IIIA metals in hydrodehalogenation reactions is dominated by the use of the corresponding and diverse hydrides. For instance, borohydrides allow hydrodechlorination of alkyl and aryl halides, albeit high temperatures are required for polychlorinated aromatic compounds. LAH is widely utilized for alkyl, vinyl, and aryl halogenated substrates, including aromatic fluorides, electron-transfer processes being proposed the most likely to occur. More hindered and less reactive aluminum hydrides achieve the transformation of acid chlorides into the corresponding aldehydes. Although less common, gallium hydrides exhibit a reactivity between those of the analogous aluminum and boron hydrides, being compatible with several functional groups. Of great interest is the use of indium metal in aqueous media, mainly for the hydrodehalogenation of α-halocarbonyl compounds under environmentally friendly conditions.

Silicon, germanium, and tin hydrides are the main reagents involved in hydrodehalogenation reactions mediated by group IVA metals, all under radical conditions. The wide variety of silicon hydrides available, including trialkylsilanes, alkylthiosilanes, disilanes, trisilanes, cyclic and aromatic silanes, or polysilanes, allow the reduction of almost all kinds of halogenated substrates. Such a diversity of hydrides is also found for tin, which shows good performance for bromides, iodides, and α-halocarbonyl compounds, one main advantage being the possibility for the hydrides to be supported on polymers.

Although only a few examples of hydrodehalogenation reactions mediated by group VA and VIA metals are reported in the literature, it is noteworthy to mention their application, primarily as metal hydrides, in the effective hydrodehalogenation of α-halocarbonyl compounds under very mild reaction conditions.

Within the transition metals, titanium and zirconium cyclopentadienyl complexes are the most used catalysts of the group IVB metals, normally in combination with Grignard reagents or metal hydrides. The corresponding transition-metal hydride species are involved in these hydrodehalogenation reactions that have been applied mainly to α-bromoketones and aromatic halides, including fluorides. Chromium hydrides as well as the carbides of molybdenum and wolframium also show good behavior in the title reaction, the carbides being especially effective in the selective hydrodehalogenation of CFCs.

Group VIIIB metals are the most important group of elements taking part in hydrodehalogenation reactions. Zerovalent metals, metal salts, complexes, supported metals, and bimetallic or multimetallic combinations, under homogeneous or heterogeneous conditions, offer a large variety of reducing systems with different properties that in some cases can be specific for a certain type of substrate. Thus, the elements of the first triad, iron, cobalt, and nickel, have been successfully utilized in hydrodehalogenation reactions under homogeneous conditions, mainly as their metallocoenzyme complexes and some biomimetic complexes in the presence of a reductant. Under heterogeneous conditions, and due to its excellent behavior in aqueous systems, elemental iron seems to be the metal of choice for larger scale applications and for groundwater remediation, being especially effective in the hydrodechlorination of highly polychlorinated compounds such as PCBs, DDT, or several pesticides. A two-electron-transfer process seems to be the most plausible for the hydrodehalogenation in aqueous systems mediated by elemental iron. Different forms of active metallic nickel have been reported, such as Raney nickel or those obtained by reduction of nickel salts using other metals of metal hydrides. The high reducing power of nickel borides, or that of active nickel in combination with molecular hydrogen or protic solvents, has been applied to the reductive hydrodehalogenation of many organic halides. Alternatively, reactions can be conducted with metallic nickel supported on silica, alumina, charcoal, or zeolites, among others, also with good effectiveness.

Concerning the second triad, ruthenium and rhodium complexes (mainly phosphine complexes) have been utilized in homogeneous catalytic hydrodehalogenation with molecular hydrogen or by transfer hydrogenation. These catalysts showed remarkable performance in the selective hydrodechlorination of carbon tetrachloride and CFCs, as well as in the hydrodehalogenation of aryl halides, allowing for instance activation of carbon−fluorine bonds. However, palladium is still the preferred transition metal, above all for laboratory-scale hydrodehalogenations, due to its unique properties and to the wide variety of palladium catalysts available, both for homogeneous and heterogeneous reactions. Phosphine-based complexes are the most commonly used palladium catalysts in homogeneous hydrodehalogenations, intermediate palladium hydride species being involved by reaction with molecular hydrogen or a metal hydride, by hydrogen transfer, or by β-hydride transfer from an organometallic reagent. Polymer-anchored monometallic and bimetallic palladium-based homogeneous catalysts have also been developed. In regard to heterogeneous conditions, few examples are reported for unsupported monometallic palladium, most of the literature covering hydrodehalogenation reactions with supported palladium catalysts. Palladium on carbon, followed by palladium on alumina with different hydrogen sources, dominate this field, the latter being very effective in the hydrodehalogenation of CFCs and chlorinated solvents (also in aqueous media). Many other supports including oxides, salts, or zeolites have also been utilized. One of the most effective ways to increase degradation rates of halogenated compounds is by using bimetallic palladium catalysts, due to a synergistic effect. In particular, palladized iron has been shown to be very useful in the transformation of chlorinated solvents and PCBs.

Within the third triad, osmium and iridium are scarcely utilized for the title reaction, whereas platinum is mostly used on supports such as carbon, magnesium oxide, or alumina under a hydrogen atmosphere, in some cases being superior to the related palladium catalysts. The activity and selectivity of platinum catalysts in the hydrodehalogenation of polychlorinated solvents can be increased by the addition of a second metal such as copper or vanadium.

Copper- and silver-mediated hydrodehalogenations are also scarce, mainly involving copper metal, copper oxide, or copper salts, on one hand, and bimetallic silver particles, on the other hand. The latter allowed efficient dechlorination methodologies of polychlorinated benzenes, PCBs, and 1,2-dichloroethane.

Elemental zinc has demonstrated a remarkable reducing ability in aqueous or protic media of such noxious materials as lindane, 1,1,1-trichloroethane, or dioxins. In addition, zinc is probably the metal of choice to achieve highly regioselective reductive defluorination of perfluoroarenes and perfluoroalkylarenes, either alone or combined with copper. Alternatively, cyclopentadienyl organolanthanide complexes in the presence of a reductant can also be used as catalysts for that purpose. Finally, samarium(II) iodide has found direct application in radical dehalogenation of cyclopropyl halides or in the reduction of α-halocarbonyl compounds through the corresponding samarium enolates.

We believe that the hydrodehalogenation reactions herein described will serve in the near future as a base to obtain more efficient and practical methodologies from a synthetic point of view, but also to allow the preservation of the environment and therefore to prolong the Earth's life.

IX. Abbreviations

ACVA	4,4′-azobis(4-cyanovaleric acid)
aq	aqueous
Arochlor	mixture of chlorinated biphenyls
Aliquat 336	tricaprylmethylammonium chloride
AFM	atomic force microscopy
AIBN	azobis(isobutyronitrile)
An	anisyl
BER	borohydride exchange resin
Boc	*tert*-butoxycarbonyl
cat	catalytic
Cbl	cobalamin
CD	cyclodextrin
CFC	chlorofluorocarbon
CFC-11	trichlorofluoromethane
CFC-12	dichlorodifluoromethane
CFC-113	1,1,2-trichloro-1,2,2-trifluoroethane
CFC-113a	1,1,1-trichloro-2,2,2-trifluoroethane
COD	1,5-cyclooctadiene
COE	cyclooctene
CoPcTs	cobalt tetrasulfophthalocyanine
CoTMPyP	cobalt tetrakis(*N*-methyl-4-pyridiniumyl)porphyrin
Cp	η^5-cyclopentadienyl
Cp′	η^5-methylcyclopentadienyl
Cp*	η^5-pentamethylcyclopentadienyl
Cy	cyclohexyl
dba	dibenzylideneacetone
DBCP	1,2-dibromo-3-chloropropane
DDD	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane
DDE	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene
DDT	1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)-ethane
DIBAL	diisobutylaluminum hydride
dippp	1,3-bis(diisopropylphosphino)propane
DMA	*N*,*N*-dimethylacetamide
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppr	1,1′-bis(diphenylphosphino)ruthenocene
DTBB	4,4′-di-*tert*-butylbiphenyl
EPA	Environmental Protection Agency
EPR	electron paramagnetic resonance
equiv	equivalent

etp	bis(diphenylphosphinoethyl)phenylphosphine
Fmoc	9-fluorenylmethoxycarbonyl
GC	gas chromatography
HBTD	hexabutylditin
HCB	hexachlorobiphenyl
hfacac	hexafluoroacetylacetonate
HCFC	hydrochlorofluorocarbon
HCFC-123	1,1-dichloro-2,2,2-trifluoroethane
HCFC-123a	1,2-dichloro-1,1,2-trifluoroethane
HFC	hydrofluorocarbon
HMPA	hexamethylphosphoramide
HP	hydroxypropyl
HPLC	high-performance liquid chromatography
IARC	Agency for Research on Cancer
LAD	lithium aluminum deuteride
LAH	lithium aluminum hydride
LAH−NMP	lithium aluminum hydride−*N*-methylpyrrolidine
LBEA	lithium *tert*-butylethylamide
LDA	lithium diisopropylamide
LDPA	lithium tetrakis(*N*-dihydropyridyl)aluminate
LiDTBB	lithium 4,4′-di-*tert*-butylbiphenylide
liq	liquid
Ln	lanthanide
Mont	montmorillonite
MS	mass spectrometry
MWs	microwaves
NiCRA	nickel-containing complex reducing agent
NMP	*N*-methylpyrrolidine
NMR	nuclear magnetic resonance
Nph	neophyl (2-methyl-2-phenylpropyl)
OeiBC	octaethylisobacteriochlorin
OSHA	Occupational Safety and Health Administration
PBB	polybrominated biphenyl
PCB	polychlorinated biphenyl
PCN	polychlorinated naphthalene
PEG	poly(ethylene glycol)
PEGMME	poly(ethylene glycol) monomethyl ether
PMB	*p*-methoxybenzyl
PMHS	poly(methylhydrosiloxane)
PPN	bis(triphenylphosphoranylidine)ammonium
PTA	1,3,5-triaza-7-phosphaadamantane
PTFE	poly(tetrafluoroethylene)
PVC	poly(vinyl chloride)
PVP	poly(*N*-vinyl-2-pyrrolidone)
Py	pyridine
Red-Al	bis(2-methoxyethoxy)aluminum hydride
rt	room temperature
sc	supercritical
SDMA	sodium dihydrobis(2-methoxyethoxy)aluminate
SDS	sodium dodecyl sulfate
SEM	scanning electron microscopy
SET	single-electron transfer
S_N2	second-order nucleophilic substitution
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TCDD	tetrachlorodibenzo-*p*-dioxin
TCDF	tetrachlorodibenzofuran
TCE	trichloroethylene
TEG	tetraethylene glycol
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy radical
THF	tetrahydrofuran
THP	tetrahydropyranyl
TIPS	trisisopropylsilyl
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylene-1,2-diamine
Tol	tolyl
TPPMS	*m*-sulfophenyldiphenylphosphine sodium salt
TPTH	triphenyltin hydride
Ts	*p*-toluenesulfonyl
UV	ultraviolet−visible
XPS	photoelectron spectroscopy
Z	benzyloxycarbonyl

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