# ChemInform Abstract: A General Survey and Recent Advances in the Activation of Unreactive Chemical Bonds by Metal Complexes

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# A General Survey and Recent Advances in the Activation of Unreactive Chemical Bonds by Metal Complexes

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## 1
## General Introduction

The activation of chemical bonds is perhaps the most important area of modern chemistry. In our never ending search for cheap raw materials, the use of abundant but traditionally unreactive molecules as synthetic precursors is becoming increasingly more attractive. A major goal of this endeavor is to devise not only better methods to produce bulk (commodity) chemicals but also to synthesize new materials for industry, medicine and research. Unreactive chemicals include compounds such as hydrocarbons and other media which, under normal circumstances, do not react with other substrates (or themselves). Two primary examples are molecular nitrogen and saturated alkanes. These substances represent very inexpensive potential sources of nitrogen and carbon, respectively. Hydrocarbons (i.e., oil and petroleum products) are the largest fraction of world primary energy production and are thus readily available starting materials. The same is true for dinitrogen as it is a major component of the earth's atmosphere. In addition, the activation of general classes of inert bonds, such as the C–Cl, C–F

or C–O bonds, has importance in the destruction of certain man-made environmental toxins (PCB's, CFC's, etc.) and in the potential application of much cheaper chlorinated compounds as reagents (e.g., in Grignard reactions). The activation of specific C–C bonds has great potential in speciality chemical synthesis as does, to a lesser extent, the Si–Si bond in materials science.

This volume of Topics in Organometallic Chemistry is devoted to recent advances in the activation, by metal complexes, of what are termed unreactive chemical bonds. In this introduction, a brief overview of each topic will be presented. This is certainly not intended as a comprehensive review of each subject but merely as a stepping stone to the more detailed chapters that follow within.

# 2
# The Activation of C–H Bonds

The synthetic utility of activating C–H bonds has long been recognized in chemistry. For example, the combustion of hydrocarbons as an energy source with the concomitant formation of water and carbon dioxide is a fundamental reaction in most machines. The *selective* activation of specific types of C–H bonds is however, by no means a simple problem. The strength of the C–H bond in for example, methane (440 kJ/mol; 105 kcal/mol) or benzene (461 kJ/mol; 110 kcal/mol), is a factor which alone does not dominate the chemistry, but it does make activation of this type of bond relative to weaker bonds present in a molecule more difficult [1]. Catalytic activation by metal containing compounds has therefore been an area of intense research.

The study of the reactivity of aryl C–H bonds began in the last century. However, direct bond activation was only observed in the last 35 years, despite the quite early successes of scientists like Charles Friedel and James Crafts who discovered (1877) that aluminum chloride catalysts can promote the alkylation of benzene. Specifically, *orthometallation* of aryl groups attached to coordinated donor atoms was among the first examples of direct C–H bond activation in a transition metal complex. This work demonstrated that an M–C(aryl) fragment and a metal hydride could be formed directly by oxidative addition of an *ortho* H–C(aryl) group [2–8]. An early example of this is the orthometallation of a coordinated triphenylphosphine ligand bound to an Ir(I) metal center [2–6]. Intermediates in this reaction have been isolated and all show close interatomic contact distances between the metal and a hydrogen nucleus. Examples include the very early crystallographic work of Laplaca and Ibers [9] of the Ru(II) complex $RuCl_2(PPh_3)_3$. Related chemistry includes examples of hydrogen atoms of alkyl groups in close proximity to a metal centre, such as the early disclosure by Maitlis and coworkers concerning a Pt phosphine compound with a close intramolecular Pt···H(alkyl) distance [10]. Crabtree and others have coined the phrase agostic to describe this type of interaction and have used these complexes as models of the intimate first stages of C–H bond activation [11, 12]. However, the direct use of aromatic compounds in synthesis is generally restricted to the activation of groups other then the C–H fragment (e.g., C–X bonds: X=Br, Cl).

Since aryl halides are fairly cheap reagents, there has been less recent emphasis (see Section 3 below) on the development of aryl relative to that of alkyl C–H bond activation [13–17]. However, the manufacture of aryl halides is not an environmentally friendly process and thus the future of bulk aromatic synthesis may lie in the direct activation of C–H bonds. For example, the formation of benzaldehyde from the insertion of CO into a C–H bond of benzene is a recent development in this area [17].

Bergman has referred to the selective activation of C–H bonds of saturated alkanes as one of last remaining Holy Grails of synthetic chemistry [18–20]. The initial (perceived) breakthrough in alkyl C–H bond activation came from the simultaneous [21, 22] but independent work of Graham and coworkers (University of Alberta, Canada) and by Bergman et al. (University of California at Berkeley, U.S.A.). Both of these groups discovered that cyclopentadienyl complexes of Ir and Rh can, under photochemical conditions, oxidatively add alkanes to yield hydridometal alkyls. Although none of these systems have yet been shown to operate catalytically, detailed study of the fundamental aspects of this chemistry have continued in earnest [23–29]. Kinetic analysis has revealed that initial agostic interactions of the alkane with the metal center is a key (reversible) intermediate step and that later oxidative addition likely occurs via a simple three-center transition state [30]. Further work in this important area of research will be disclosed in the later chapters of this text by Prof. W. D. Jones (Stoichiometric Activation of C–H Bonds), Prof. F. Kakiuchi and Prof. S. Murai (Catalytic Activation of C–H Bonds) and the chapter by Prof. A. Sen (Catalytic Activation of Methane and Ethane by Metal Compounds).

# 3
# The Activation of C–Cl and C–F Bonds

The activation of chlorinated hydrocarbons is an area of study that has direct environmental consequences in relation to the facile destruction of polychlorinated biphenyls (PCB's C–Cl bond strength 402 kJ/mol; 96 kcal/mol for $C_6H_5$–Cl ) and other pollutants. The high reactivity of simple polyhalogenated alkanes such as tetrachloromethane [31–33], is generally facilitated by the ease of formation of the trichloromethane radical. However, other chlorocarbons are not so easily activated. There are a few examples of metal complexes which contain coordinated alkyl halides [34–37] and these may be considered as agostic interactions (i.e., M···X–R) between the metal and an alkyl halide atom. Direct oxidative addition of unreactive haloalkanes such as dichloromethane has been reported [38, 39]. The activation of C–Cl bonds will be described in the chapter by Dr. V. V. Grushin and Prof. H. Alper (Activation of Otherwise Unreactive C–Cl Bonds) which details the use of chlorocarbons for a variety of applications in synthesis. The environmental (e.g., ozone depletion) and potential pharmaceutical relevance of fluorocarbons has made C–F bond activation an area of quite active research. Despite the high energy of C–F bonds (e.g., 644 kJ/mol; 154 kcal/mol for the C–F bond in $C_6F_6$), the activation of this fragment by a

number of complexes has been reported [40, 41]. Many metal complexes can activate C–F bonds in a stoichiometric fashion and the list includes reagents containing Ti [42], Fe [43], Ni [44], Ru [45, 46], Rh [47–50], Ir [47–50], W [51], U [52] and Yb [53]. Recently, this area has expanded to the catalytic activation of C–F bonds as reported by Aizenberg and Milstein [54, 55]. The use of electron-rich Rh phosphine compounds enables the activation of fluorobenzenes, although turnover numbers are low (<1 turnover per hour at 94 °C) [54]. Further details on this chemistry can be found in the relevant chapter by Prof. T. G. Richmond (Metal Reagents for Activation and Functionalization of C–F Bonds).

## 4
## The Activation of C–C and Si–Si Bonds

The activation of C–C bonds (specifically cleavage reactions) by metal compounds has been extensively studied and there are many reagents that can be used to perform the selective manipulation of alkynes and alkenes to produce a plethora of new compounds [56–59]. Transition metal and lanthanide complexes are playing an ever increasing role in the selective formation and cleavage of C–C bonds [60]. Considerable effort has been applied to the application of metal compounds in such diverse areas as ring forming reactions [61–64], regio- and enantio-selective addition reactions [65–71], direct C–C bond formation [72–76] and other processes [56, 57, 77]. This represents a very large cross section of chemical reactivity and the review in this text by Dr. M. Murakami and Prof. Y. Ito (Cleavage of C–C Single Bonds by Transition Metals) will emphasize this selected area of organometallic chemistry and (homogeneous) catalysis.

A related area of this chemistry is the selective reactivity of Si–Si bonds [78]. The use of disilanes in organic synthesis for the creation of new (and reactive) Si–C bonds is an area of current interest and application [79–81]. This work has stemmed from earlier studies which have demonstrated that disilanes readily oxidatively add to a variety of metal centres [82] to produce transition metal silyl complexes [83]. The investigation of this area will be detailed by Prof. M. Sugimone and Prof. Y. Ito (Activation of Si–Si Bonds: Stoichiometric and Catalytic Reactions).

## 5
## The Activation of C–O Bonds

The cleavage of C–O bonds has significant applications in a number of important areas of synthetic organic and organometallic chemistry [56, 57, 83, 84]. The activation of carbon-oxygen single, double and triple bonds has been an area of active research in relation to catalysis and to many fundamental chemical reactions [85]. The reactions of carbon monoxide or dioxide has long been recognized in organometallic chemistry and thus can not be considered unreactive substrates by the definition of this book. Other organic compounds which contain the C=O functionality such as aldehydes and ketones can also not be con-

sidered unreactive as per the definition of this manusript [84, 85]. However, asymmetric reactions at this functional group is an area of great current interest. Specifically, Prof. Y.-S. Lin and Prof. A. Yamamoto will describe recent advances in the activation of the important allylic C–O bond with special detail paid to allyl metal complexes. The allylic functionality has been studied extensively because of its importance in a number of specialty organic syntheses [86–92]. In addition, the chapter "Activation of C–O Bonds. Stoichiometric and Catalytic Reactions" will review recent applications of transition metal compounds to the cleavage of C–O bonds of esters, ethers [91, 92] and anhydrides. The rupture of the C–O multiple bonds is also detailed.

## 6
## The Activation of Molecular Dinitrogen

Catalytic dinitrogen activation has been one of the most difficult challenges in the field of organometallic chemistry. Nitrogen gas is used as the N-containing feedstock in the (high temperature and pressure) Haber process for the production of ammonia. The drastic conditions that are necessary for efficient catalysis has lead to a vast amount of study directed towards the design of a mild ammonia synthesis from $N_2$. The very high strength of the N–N bond (945 kJ/mol; 226 kcal/mol) and the differences in energy distribution between the bonds of $N_2$ compared with acetylene for example, lead to few similarities in the reactivity of these compounds [93–96]. Dinitrogen is a very weak base and hence does not easily (or strongly in most cases) coordinate to metals. The first example of an $N_2$ complex was not isolated until 1965 by Allen and Senoff [97]. Since that time, dinitrogen complexes have been isolated for almost all of the transition metals and lanthanides. However, simple coordination of $N_2$ did not immediately lead to any activation of the molecule. It took several years before a simple $N_2$-compound could even be stoichiometrically converted to hydrazine [98]. The most promising results in this area have been reported by Laplaza and Cummins [99]. Their 1995 disclosure was the first example of a mild, catalytic conversion of $N_2$ to ammonia using a high valent Mo complex as catalyst [100]. The chapter presented by Prof. M. Hidai and Prof. Y. Mizobe entitled "Activation of the N–N Triple Bond in Molecular Nitrogen: Toward its Chemical Transformation into Organo-nitrogen Compounds" will discuss recent work concerning direct organonitrogen synthesis using transition metal catalysts.

## 7
## Concluding Remark

The use of metal compounds in the activation of chemical bonds is an area of useful and fascinating research [101]. The following chapters will detail many of the recent advances in this area of chemistry with the emphasis on the use of traditionally unreactive substrates.

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