

Thesis at a Glance

“Fresh ideas have always been a necessary ingredient for progress in chemistry.....” –Fritz Vögtle, J. Fraser Stoddart and Masakatsu Shibasaki in *Stimulating Concepts in Chemistry*, Wiley-VCH, 2000

One such stimulating idea which is continuously inspiring chemists during the recent times in the field of organic transformations and fine chemical syntheses is the concept of “*Cooperative Bimetallic Catalysis*” (By virtue of its astonishing capability through a win-win paradigm, the cooperative bimetallic catalysis is developing dramatically in almost every corner of organic transformations, from substitution to addition, cyclization to coupling and many more.)

Looking at the rapid exploration of the cooperative catalysis two curious questions should appear immediately in our mind – *why* and *how*? The answer will eventually signify the genesis of this stimulating concept of cooperativity. Briefly, we can say that the interplay of synergism between two or more adjacent active metal centers in combined dual-metal or single bimetallic catalyst leads to the enhanced reactivity of substrates through their selective and proximal binding/activation in a geometrically suitable environment. The final outcome of such a synergy is an organic transformation leading to product formation with very high selectivity, and (once tuned) with high catalytic efficiency. Therefore, (the strategy of utilizing cooperative bimetallic catalysts having finely tuned active sites has been considered as a very powerful and highly demanding and equally challenging in homogeneous catalysis.)

The field of aromatic alkylation, both Friedel-Crafts (FC) and non-FC types, is extremely important for the synthesis of various useful chemicals at bench-scale as well as in industries. In view of this, sustained attention is given to improve the rate, efficiency, substrate scope and product selectivity of this reaction. So far, such improvement mostly relied on *non-cooperative* type of catalysts. Certainly, one should expect to add a valuable contribution into aromatic alkylation by invoking the concept of *cooperative bimetallic catalysis*.

Based on the above background, the major objective of the present work is to initiate an exploration towards the design and reactivity of new cooperative bimetallic

catalysts for aromatic alkylation. Yet another task set for the present work is to investigate the catalytic cycle in general and the substrate activation stage in particular.

Along the above goal, the thesis entitled ***“Designing Cooperative Catalysts within Ir–Sn Regime: Synthetic & Mechanistic Studies towards Aromatic Alkylation”*** embodies work directed towards the multi-prong aspects of a cooperative bimetallic catalysis concept towards aromatic alkylation. The thesis is divided into the following seven chapters:

Chapter 1. Dual-metal/Bimetallic Catalysis in Homogeneous Regime for Fine Chemical Synthesis: An Overview

Chapter 2. Catalytic Aromatic Alkylation: Current Status & Objective of the Present Study

Chapter 3. Synthesis of Transition Metal–Tin Heterobimetallic Complexes by Oxidative Addition & Their Characterization

Chapter 4. Cooperative Catalysis by Transition Metal–Tin Heterobimetallic Complexes: Alkylation of Aromatics by π -Activated Alcohols

Chapter 5. Mechanistic Aspects of the Cooperative “Ir–Sn” Catalyzed Aromatic Alkylation: Kinetics & Spectroscopic Studies

Chapter 6. Experimental

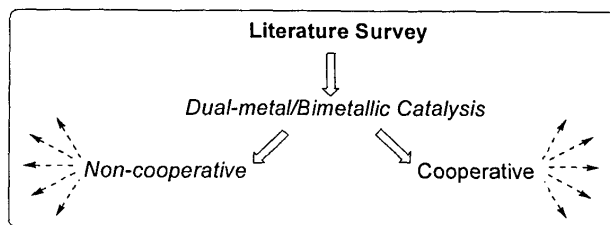
Chapter 7. Conclusion & Scope

A brief highlight on the major deliberations of chapters 1-5 is presented below to glean insight into the overall aspect of the thesis.

Chapter 1. Dual-metal/Bimetallic Catalysis in Homogeneous Regime for Fine Chemical Synthesis: An Overview

In this chapter a short review is presented on the conceptual evolution, recent developments and applications of the dual-metal/bimetallic cooperative catalysis. This type of novel bimetallic cooperative concept has manifested itself quite impressively in the field of homogeneous catalysis. A rapid upsurge of the application of bimetallic cooperative catalysis continues to bring forth more and more examples today with a parallel competition from the well-established monometallic counterpart.

Figure 1 *Exploration of Dual-metal/Bimetallic Catalysis*

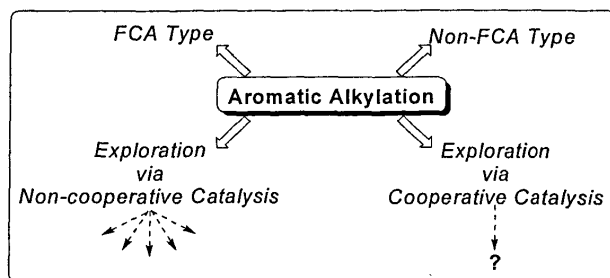


“Dual-metal/bimetallic” catalysis is referred to as a catalytic process, which uses two distinct metal centers for substrate binding. The said centers may be grafted within a single motif, or are added as two separate molecular units. We have referred the former case as “**intramolecular dual-metal/bimetallic**”, while the later as “**intermolecular dual-metal/bimetallic**”. It is point worthy that either of the above catalysis may or may not involve cooperation between the two metal centers during substrate activation. Cases where two metals act synergistically during the substrate activation and coupling steps in the catalytic cycle are defined as “**cooperative catalysis**”. Whereas, if the two metals operate independently in the catalytic cycle and deliver their individual functions i.e., if there is no synergy between them during substrate activation steps, then it is classified as “**non-cooperative catalysis**”. In the later case, often one metal partner is a transition metal catalyst and the other metal compound may serve various roles. The chapter provides a detailed account on the status of all of the above concepts with examples drawn from recent literature.

Chapter 2. Catalytic Aromatic Alkylation: Current Status & Objective of the Present Study

This chapter overviews the current status of catalytic aromatic alkylation (CAA) via Friedel–Crafts (FC) and non-FC catalysts.

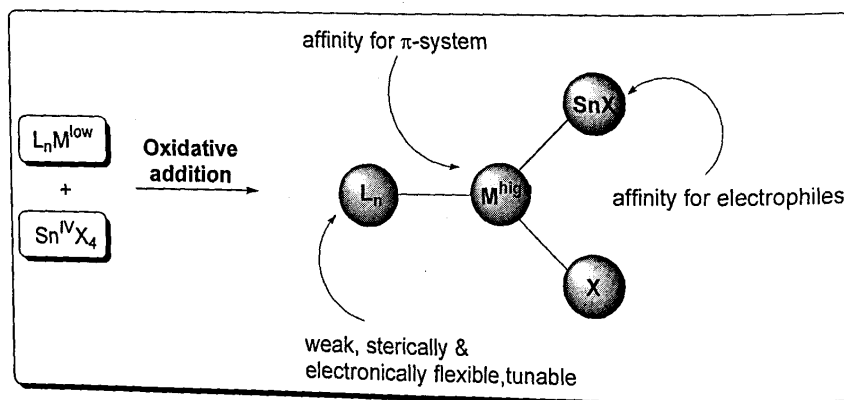
Figure 2 *Schematic Diagram of Current Status of CAA*



The presented analyses indicate that in spite of their outstanding capabilities, many (but not all) FCA-processes still evoke considerable interest. The challenging goal in them is to achieve a clean and highly selective homogeneous FCA protocol. On the other hand, in the field of aromatic functionalization, transition metal catalysts are known mainly for non-FC type of reactions (like hydrophenylation and allylic alkylation) with fewer examples of aromatic alkylations. It is remarkable to note that so far the concepts and examples largely relied on monometallic catalysis.

The above realization profoundly helped us to set forth the objectives in the present thesis in line with the concept of bimetallic cooperative catalysis. A plausible heterobimetallic catalyst design strategy based on **hard metal–soft metal** combinations has been propounded for investigation in the thesis. The combinations proposed for investigation is a high valent late transition metal–tin motif designed via oxidative-addition reaction.

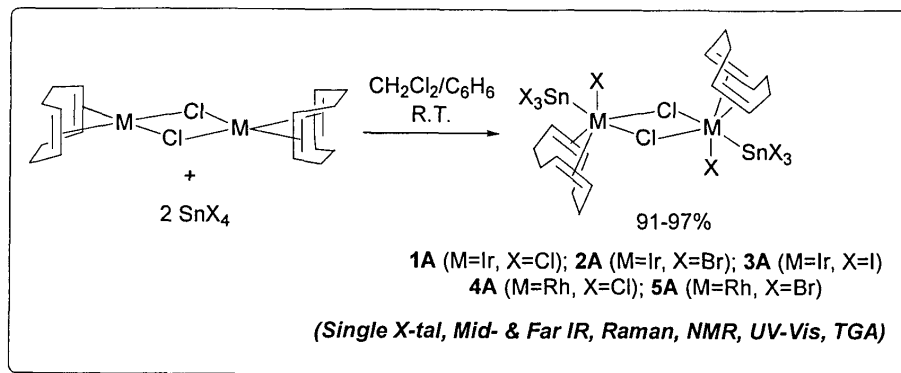
Figure 3 Feature of a High-valent M–Sn Motif



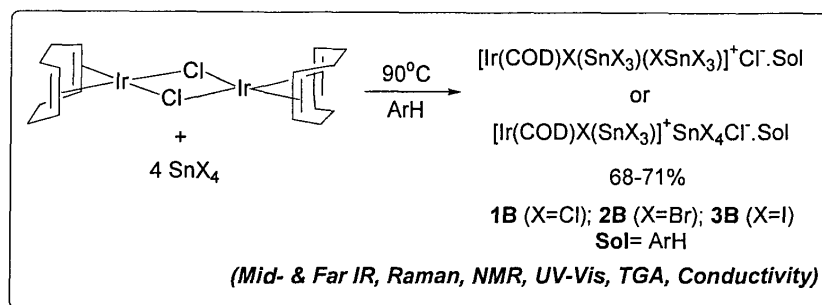
Chapter 3. Synthesis of Transition Metal–Tin Heterobimetallic Complexes by Oxidative Addition & Their Characterization

This chapter describes the synthesis of transition metal–tin heterobimetallic complexes. As shown in Schemes 1 & 2, the oxidative addition of SnX_4 compounds across low-valent Rh^I and Ir^I olefin complexes generates two types of complexes at two different well-standardized reaction conditions. The complexes contain high-valent Lewis acidic transition metal–tin core with metal–metal bonds. This unique feature has been proved to be valuable for their catalytic activity.

Scheme 1



Scheme 2

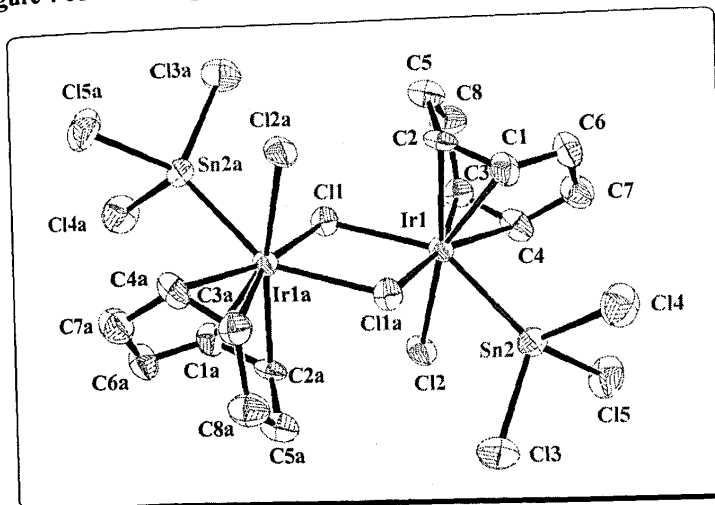


Single-crystal X-ray structures have been determined for the complexes **1A** and **2A**. This confirms the cis-addition of Sn–X bond and retention of the halo–bridge in the final complexes. Important crystal data and ORTEP diagram of **1A** have been shown here (Table 1 and Figure 4).

Table 1 Important Crystal Data of **1A**

Formula	$\text{C}_{16}\text{H}_{24}\text{Cl}_{10}\text{Ir}_2\text{Sn}_2$	Formula Wt.	1192.63
Crystal System	Triclinic	Space Group	P-1
a, b, c (Å)	7.51(2), 8.08(2), 12.98(2)	V (Å ³)	773(3)
α, β, γ (deg)	80.83(7), 83.69(8), 87.54(6)	Z	1

Figure 4 ORTEP Diagram of 1A with 50% Probability Thermal Ellipsoids

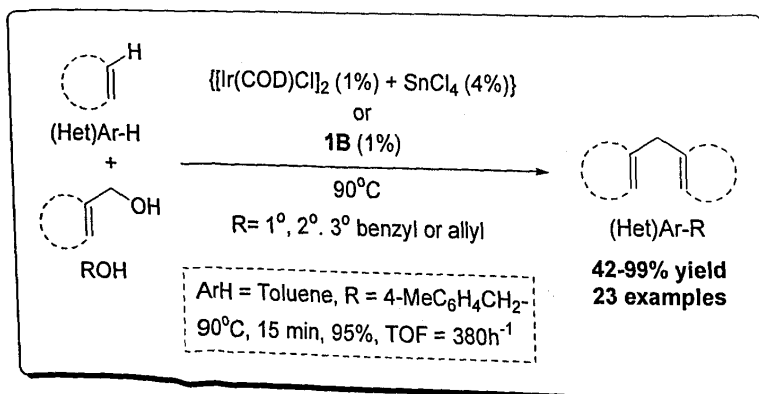


Extensive efforts have been executed to characterize the new complexes by C,H-analyses, Far- and Mid-IR, Raman, ^1H , & ^{13}C NMR, UV-Vis, TGA, and Conductivity studies. Comparative analyses of the accrued results have been done in each and every case.

Chapter 4. Cooperative Catalysis by Transition Metal–Tin Heterobimetallic Complexes: Alkylation of Aromatics by π -Activated Alcohols

This chapter presents the delightful results of the applications of the synthesized “Ir–Sn” heterobimetallic complexes towards the alkylation of arenes and heteroarenes by π -activated $1^\circ/2^\circ/3^\circ$ alcohols (Scheme 3).

Scheme 3



Model study indicates distinct cooperative effect between the two metal centers for efficient catalysis, as neither the iridium precursor complex $[\text{Ir}(\text{COD})\text{Cl}]_2$ nor the Lewis acid SnCl_4 are individually effective in this reaction (Scheme 4, Table 2).

Scheme 4

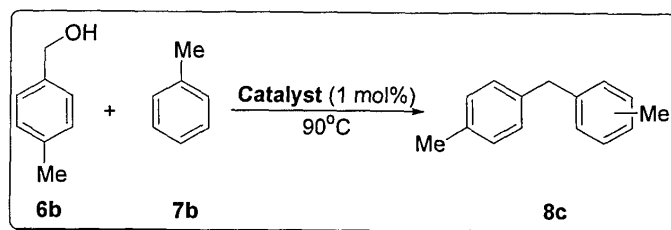


Table 2 Model Study for the Benzylation of Toluene (7b) with 4-Methylbenzyl Alcohol (6b) at 90°C

Catalyst	Time (min)	Yield (%)	TOF (h ⁻¹)
SnCl_4	360	<1	<0.2
$[\text{Ir}(\text{COD})\text{Cl}]_2$	360	0	0
1A	15	10	40
1A	360	45	7.5
1B	15	95	380

In search of other effective bimetallic combination, control studies have been performed to screen a number of other transition metal complexes and Lewis acidic metal compounds. Expectedly, some of them have been found to be moderately active with a TOF value lower than that of the best “Ir–Sn” catalyst **1B** (Scheme 5, Table 3).

Scheme 5

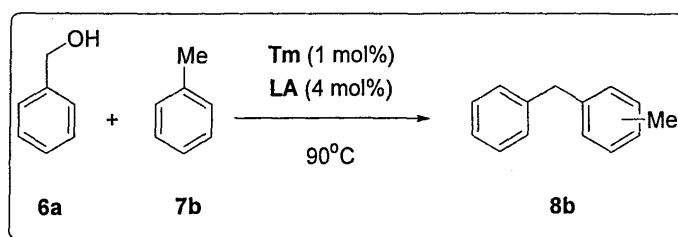
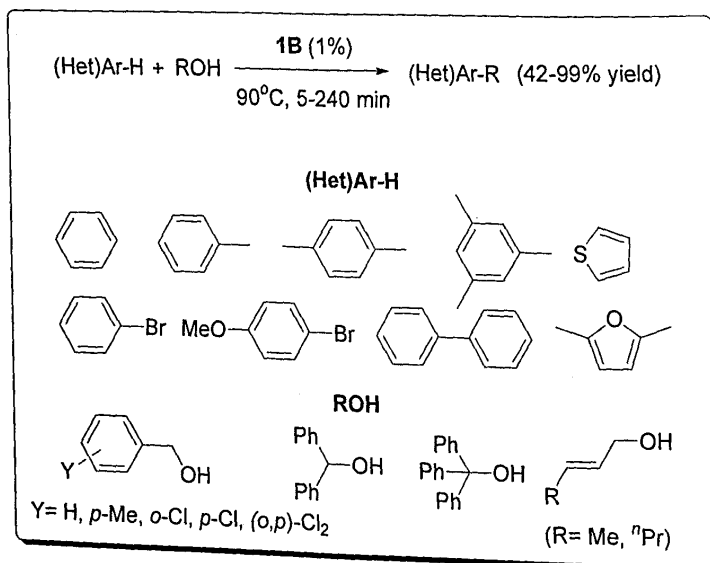


Table 3 Screening of other Transition Metal/Lewis Acid Metal Catalyst Combination

Tm	LA	8b after 15 min (%)	8b after 180 min (%)
[Ir(COD)Cl] ₂	SnCl ₄	94	95
RhCl(CO)(PPh ₃) ₂	SnCl ₄	5	94
RhCl(PPh ₃) ₃	SnCl ₄	8	85
[Rh(COD)Cl] ₂	SnCl ₄	0	8
[Ir(COD)Cl] ₂	BF ₃ ·OEt ₂	0	5
[Ir(COD)Cl] ₂	AlCl ₃	0	2
[Ir(COD)Cl] ₂	SnCl ₂	0	2
[Ir(COD)Cl] ₂	TiCl ₄	0	0

The reaction scope has also been tested for the coupling of various types of electron-rich as well as deactivated arenes and heteroarenes with a number of π -activated 1°/2°/3° benzyl and allyl alcohols (Scheme 6). Curiously, in-situ generated as well as freshly prepared **1B** has resulted higher TOF than aged catalyst.

Scheme 6



Majority of the reactions has resulted in selective formation of the desired product with high TOF. Some specific cases of limitations of this catalysis have also been noted and explained.

Chapter 5. Mechanistic Aspects of the Cooperative “Ir–Sn” Catalyzed Aromatic Alkylation: Kinetics & Spectroscopic Studies

The successful demonstration of the catalytic application of the cooperative bimetallic “Ir–Sn” catalysis towards aromatic alkylation presented in *Chapter 4* has prompted us to investigate the mechanistic details in order to find out a conceptual gateway for further improvement in the field. Thus the proposed “*cooperative activation & coupling model*” (Figure 5) has been evaluated by analyzing results from kinetics and spectroscopic studies (Figure 6).

Figure 5 Proposed Cooperative Activation & Coupling Model

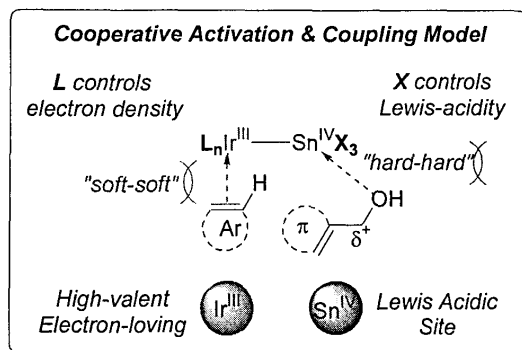
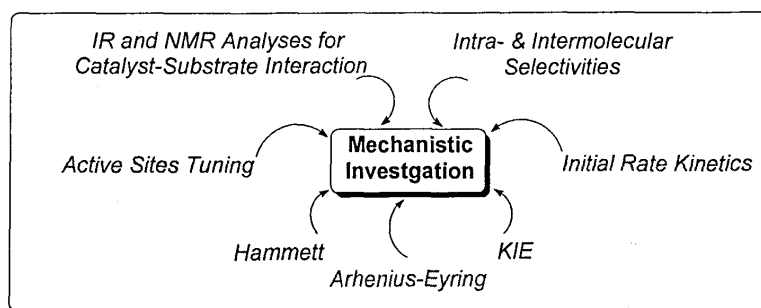


Figure 6 Mechanistic Investigation Diagram

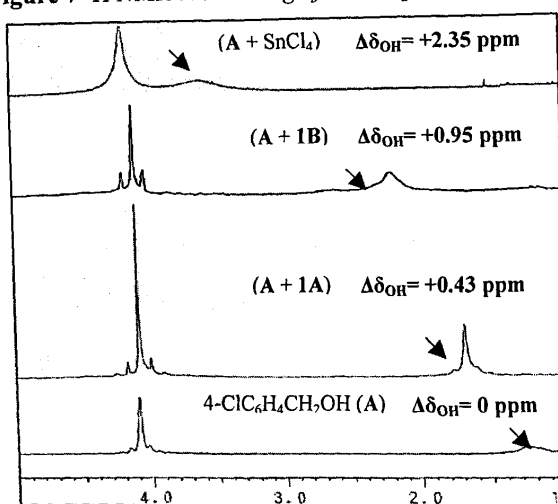


Among many characteristic features of the “Ir–Sn” catalyzed alkylation reaction evaluated so far, a few important aspects have been highlighted below:

(i) *Activation of the electrophiles at the Lewis acidic tin center as demonstrated by spectroscopic studies*

The ^1H NMR spectroscopic investigation in C_6D_6 at 25°C suggests the strength of the interaction/complexation between the alcohol and the catalyst in the order of $\text{SnCl}_4 > \mathbf{1B} > \mathbf{1A}$ (Figure 7). The largest shift of the OH proton ($\Delta\delta_{\text{OH}}$ in ppm) with only SnCl_4 compared to the other “Ir–Sn” species clearly indicates preferential activation of the electrophile at the Sn-center.

Figure 7 ^1H NMR Monitoring of Electrophile Activation

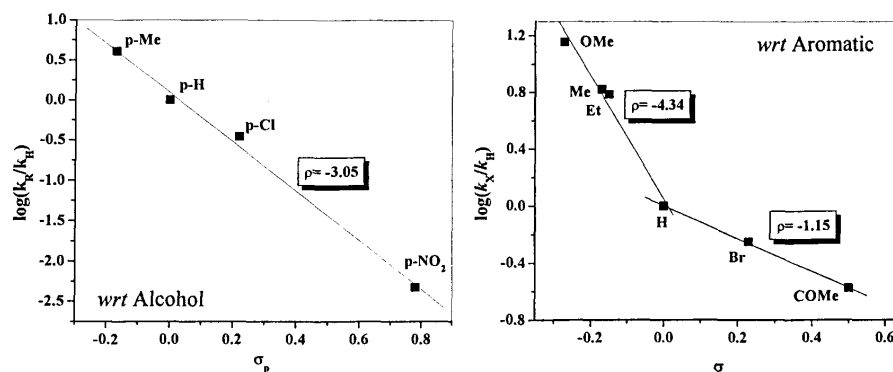
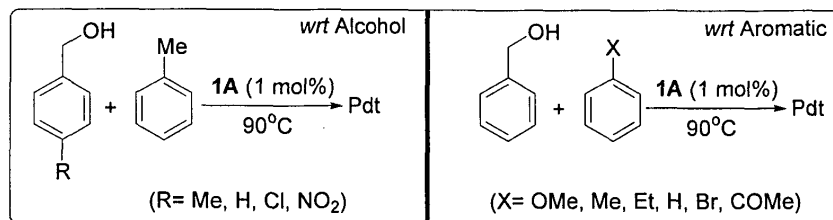


(ii) *Electrophilic Friedel-Crafts type alkylation as indicated by Hammett studies on alcohol and arene*

Hammett study on alcohol has resulted in a negative reaction constant (ρ) value (Figure 8), which proves an electrophilic mechanism for the reaction. The moderate value (-3.05) of ρ indicates the generation of weak positive charge (δ^+) on the hydroxy-bearing carbon center of the alcohol, plausibly due to the coordination of the oxygen atom of the $-\text{OH}$ group to the Sn-center of the catalyst. On the other hand, the Hammett study on aromatic substrate is very interesting (Figure 8). For electron rich arenes the ρ value has been determined as -4.34 while for deactivated arenes it is -1.15. Both the negative values indicate the expected electron-flow out of the aromatic ring as in electrophilic mechanism. But in the first case there may be formation of arenium type intermediate where the positive charge is delocalized round the aromatic ring, while in

the latter case a concerted mechanism may involve with π -electron overlap and some loss of conjugation of the aromatic ring.

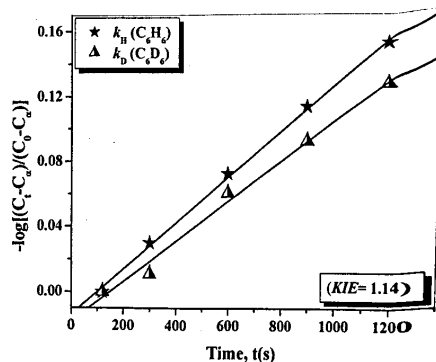
Figure 8 Hammett Study on Alcohol & Aromatic



(iii) Absence of aromatic C–H activation pathway as established by kinetic isotope effect (KIE)

To evaluate whether aromatic C–H bond activation involves in this reaction the kinetic isotope effect has been studied for the arene substrate during its reaction with the benzyl alcohol (Figure 9). The rate constant values k_H and k_D have been determined for C_6H_6 and C_6D_6 . The resulting small secondary kinetic isotope effect ($k_H/k_D = 1.14$) suggests the absence of C–H activation/breaking in the rate-limiting step; instead loosening of the C–H bond is likely in the transition state of the reaction.

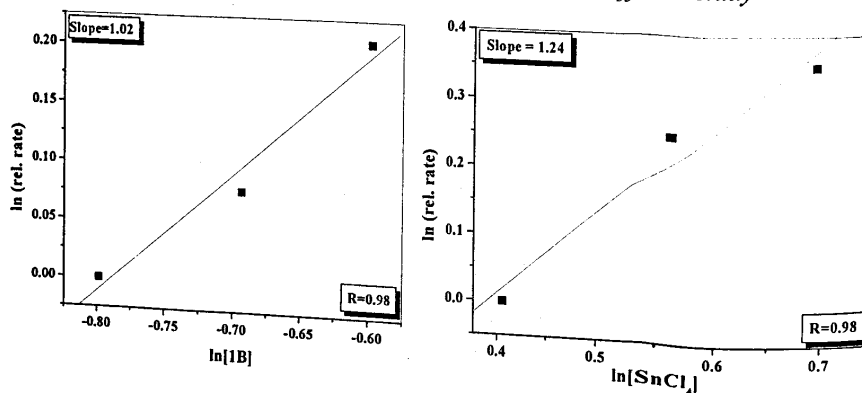
Figure 9 KIE Study on Aromatic



(iv) Cooperative effect of iridium and tin centers during substrate activation and coupling as suggested by initial rate kinetics method

Initial rate kinetics for the alkylation of benzene with benzyl alcohol at 90°C has resulted different initial rates values when the total concentration of iridium and tin were varied alternatively keeping the other parameters constant. The logarithm plots reveals first order rate dependency on both Ir-center (represented by **1B**) and Sn-center (represented by $SnCl_4$) indicating that both the metal centers cooperatively participate towards substrate activation in the rate-determining step (Figure 10).

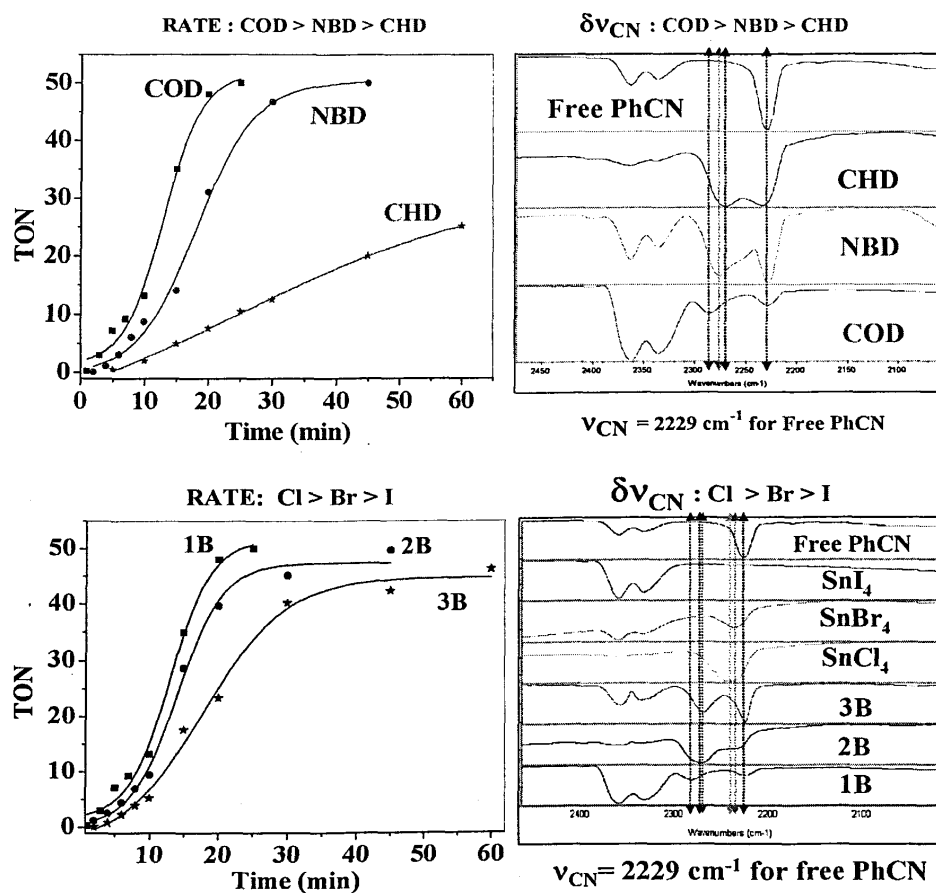
Figure 10 Logarithm Plots for Cooperative Effect Study



(v) Understanding the relation between catalytic activity and stereo-electronic influence at the active sites as suggested by ligand-variation

The diene ligand at the iridium center has been varied from 1,5-cyclooctadiene (COD) to 2,5-norbornadiene (NBD) and 1,3-cyclohexadiene (CHD) to alter the electrophilicity of Ir^{III} center, which has been monitored by IR using PhCN as a probe. This variation has been reflected in the alkylation efficiency order of the catalysts for the ligands as COD > NBD > CHD. Similar study by varying the halogen atom (X) at Sn-center has shown that both Lewis acidity, as well as TOF are in the order of Cl > Br > I. The above studies indicate the plausibility of further tuning the TOF by suitably controlling the electrophilicity at the iridium center and Lewis acidity at the tin center (Figure 11).

Figure 11 Correlation Study between Catalytic Activity and Stereo-electronic Influence at the Active Sites



All of the above studies along with several other perspectives of this reaction have been explained and elaborated in this chapter with the aid of adequate kinetic and spectroscopic data.