Ir/Sn dual reagent catalysis for the alkylation of arenes with benzyl alcohols: Kinetic evidence for an electrophilic pathway and a guide towards electronic tuning of catalyst efficiency

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Abstract

Presented herein is a detailed account of the $[Ir(COD)(\mu\text{-Cl})]_2/SnCl_4$ dual reagent catalyzed alkylation of arene/heteroarene with benzyl alcohols [J. Choudhury, S. Podder, S. Roy, J. Am. Chem. Soc. 127 (2005) 6162]. A high-valent heterobimetallic complex namely $[Ir^{III}(COD)(\mu\text{-Cl})(SnCl_3)Cl]_2$ (isolated from $[Ir(COD)(\mu\text{-Cl})]_2$ and $SnCl_4$) could also promote the alkylation. A working model on substrate binding, activation and coupling across Ir/Sn catalyst is proposed considering the hard–soft nature of the two metals (Ir and Sn) and the organic substrates (arene and alcohol). The *"tin–alcohol"* hard–hard interaction is indicated by the alkylation rate for $PhCH_2$-Y which varied with the HSAB donor strength of Y in the order OH > OAc > OMe > OC(O)H > Cl. Hammett studies with respect to arene and alcohol indicate an electrophilic mechanism. A small secondary kinetic isotope effect ruled out a C–H activation pathway. Competitive and non-competitive rate studies (isomer distribution and k_T/k_B ratio) showed a similarity with Friedel–Crafts like kinetics. Temperature dependent kinetics showed that the reaction is characterized by a positive enthalpy of activation, and small negative entropy of activation. The stereoelectronic influence of the two metal centers on the catalyst efficiency is also studied. It is shown that the coordinated ligand at the iridium center and the Lewis acidity at the tin center control the efficiency of the Ir/Sn catalysts towards aromatic alkylation.

1. Introduction

Heterobimetallic catalysis constitutes an important sub-area within the broader domain of multimetallic catalysis. The successful design of homogeneous heterobimetallic catalysts is a topic of ongoing interest [1–5]. This is due mainly to the fact that the incorporation of two metals in a single scaffold offers selective substrate binding, dual and synergistic activation, as well as enhanced reactivity [6,7]. The success of such type of catalysts depends on the properties of the two metals, and their ability to communicate electronically during substrate binding and activation. In practice, two design features exemplify such a heterobimetallic regime. The first type is an intramolecular version involving a single catalyst in which two different metals are built on a single scaffold (M–L–M′ or L–M–M′–L′). The

second type is an intermolecular version involving dual partners (M–L + M′–L′), both of which participate in the transition state [6] (Fig. 1).

In the course of our continuing effort to exploit the organic reactivity of bimetallic/dual reagent systems having transition metal (Tm) and tin (Sn) as partners [8–21], we recently communicated the first example of a heterobimetallic catalyst design within "Ir–Sn" regime for the alkylation of aromatics with benzylic alcohols [8]. It may be noted that alkylative coupling of an arene and alcohol is a classical and industrially important reaction, which has been studied with traditional Lewis acid catalysts, rare-earth triflates, $H_2PtCl_6 \cdot 6H_2O$, modified clays, and Nafion-H at 10–120% loading in the temperature range of 80–120 °C [22–26]. According to our proposal the oxidative addition of tin(IV) halides across a low-valent late transition metal organometallic partner would generate a high-valent Tm–Sn bimetallic scaffold. This scaffold bears interesting features for potential application within cooperative catalysis regime. These features include (i) a high-valent and soft

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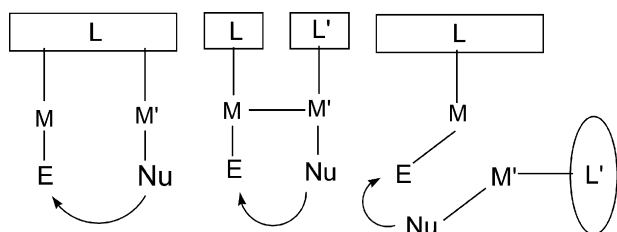 *E-mail address:* sroy@chem.iitkgp.ernet.in (S. Roy).

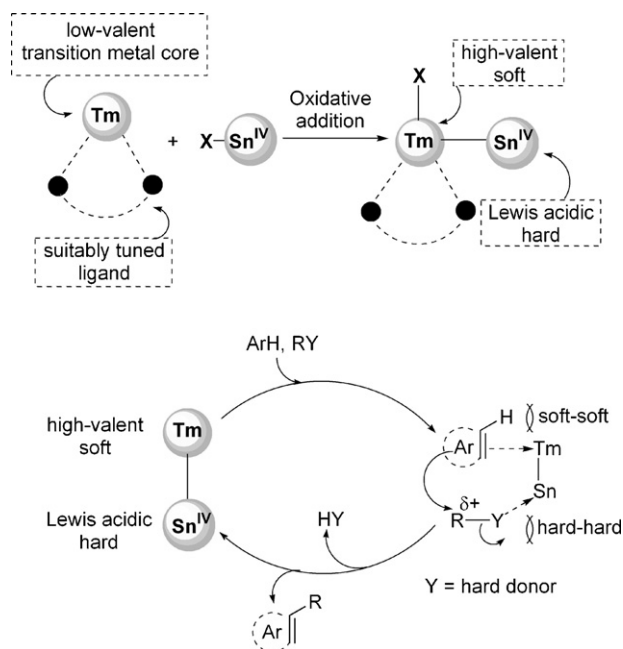Fig. 1. Intramolecular and intermolecular heterobimetallic catalysts.

Fig. 2. Proposed model on the generation and reactivity of high-valent Tm–Sn heterobimetallic motif.

electrophilic late transition metal center (Tm) for the activation of soft nucleophiles such as a π-system, (ii) a hard Lewis acidic tin center (Sn^{IV}) for the activation of substrates having hard donor atoms and (iii) close proximity of Tm and Sn centers for proximal binding and subsequent coupling between different organic substrates (Fig. 2).

Herein we present a detailed account of our results on aromatic alkylation with benzyl alcohols via Ir/Sn catalysis. We mainly focus on kinetic evidences that entailed us to glimpse on the substrate activation modes, initial bond-breaking/bond-making steps, and the interplay of stereoelectronic influence across the two metal centers, which controls the catalyst efficiency.

2. Experimental

2.1. General method

All preparations and manipulations were performed under a dry, oxygen-free argon atmosphere using standard vacuum lines and Schlenk techniques. All solvents, used for the synthesis, were dried and distilled by standard methods and previously deoxygenated in the vacuum line. Pre-coated silica gel 60F$_{254}$

(Merck) was used for thin layer chromatography and silica gel 100–200 mesh (SRL) was used for column chromatography. $IrCl_3 \cdot xH_2O$ (Arora Mathey Ltd.), 1,5-cyclooctadiene (Aldrich), 2,5-norbornadiene (Lancaster), and tin tetrachloride (Fluka) were commercially available. $SnBr_4$ [27], SnI_4 [27], [Ir(COD)(μ-Cl)]$_2$ [28], [Ir(NBD)$_3$Cl]$_n$ [29], Ir(CHD)$_2$Cl [30] and [Ir(COD)$_2$(SnCl$_3$)] [31] were prepared by literature procedure. Synthetic procedure and X-ray structure of [Ir(COD)(μ-Cl)(SnCl$_3$)(Cl)]$_2$ were reported in our previous communication [8].

^{1}H (200 MHz) and ^{13}C NMR (54.6 MHz) spectra were recorded on Bruker-AC 200 MHz spectrometer at 300 K. IR spectra were obtained using a Thermo Nicolet FTIR Spectrometer (NEXUS-870). Elemental analyses were performed on Perkin Elmer Instruments 2400 Series II CHNS/O Analyzer.

2.2. General note on GC analysis

GC analyses were on a Chemito-8610 instrument equipped with a FID using 6 ft × 1/8 in. × 2 mm SS 10% Silicone OV-1 packed column (from Chrompack), and 30 m × 0.25 mm i.d. × 0.25 μm TR-1 capillary column (from Thermo Electron, UK).

For the kinetics study, the relevant parameters were as given:

Column	6 ft × 1/8 in. × 2 mm SS 10% Silicone OV-1 packed column
Injection temperature	130 °C
Detector temperature	240 °C
Oven temperature program	80 °C–1 min–5 °C/min–100 °C–20 °C/min–160 °C–20 min
Carrier gas (N$_2$) flow	1.9 bar
Retention time (min)	
Diphenylmethane	11.5
Benzyltoluenes	14.4
Ditolylmethanes	18.5
4-Chlorodiphenylmethane	18.9
4-(Chlorophenyl)tolylmethanes	25.9

For the analysis of the other coupling products a common isothermal oven temperature could not be used due to the difference in volatility and nature of the compounds. Therefore, these were subjected to different temperature programming for the oven temperature whichever was found appropriate and matched with standard samples.

For example, to determine the *ortho*:*para* isomer ratio of benzyltoluenes, ditolylmethanes, and (4-chlorophenyl)tolylmethanes the following procedure was adopted:

Column	6 ft × 1/8 in. × 2 mm SS 10% Silicone OV-1 packed column
Injection temperature	130 °C
Detector temperature	240 °C
Oven temperature program	50 °C–10 min–5 °C/min–100 °C–2 °C/min–120 °C–1 °C/min–140 °C–15 min
Carrier gas flow	1.8 bar
Retention time (min)	
2-Benzyltoluene	45.77
4-Benzyltoluene	46.60

2,4′-Ditolylmethane	55.19
4,4′-Ditolylmethane	56.52
(4-Chlorophenyl)-2-tolylmethane	50.38
(4-Chlorophenyl)-4-tolylmethane	54.73

2.3. Isolation of [Ir(COD)(μ-Cl)Cl(SnCl₃)]₂

To a solution of [Ir(COD)(μ-Cl)]₂ (34 mg, 0.05 mmol) in dichloromethane (3 mL) was added very slowly a solution of SnCl₄ (14.7 μL, 0.125 mmol) in benzene (200 μL) under an argon atmosphere. The mixture was left undisturbed for 24 h. Deep red crystals were isolated from the reaction mixture, which were filtered, washed with benzene and vacuum-dried. Yield: 58 mg (97%). ^{1}H NMR (200 MHz, DMSO-d6) δ (ppm) = 1.71–1.79 (br, m, 8H, –CH_2), 2.21–2.26 (br, m, 8H, –CH_2), 4.16 (br, s, 8H, =CH). ^{13}C NMR (DMSO-d6) δ (ppm) = 30.7 (–CH₂), 73.6 (=CH). ^{119}Sn NMR (149.2 MHz, DMSO-d6) δ (ppm) −624. IR (KBr, cm^{-1}) 1329(s), 1433(s), 1469(m), 1617(s), 2850(w), 2907(m), 2954(m), 3010(w). Anal. Calc. for C₁₆H₂₄Cl₁₀Sn₂Ir₂·CH₂Cl₂: C, 15.98; H, 2.05. Found: C, 15.88; H, 2.03.

2.4. General procedure for screening of the catalytic efficiency of various catalysts toward alkylation of aromatic (vide Section 3.1)

A 25-mL Schlenk flask equipped with a magnetic bar, was charged with catalyst (0.01 mmol), toluene (2 mL, 18.8 mmol), and n-nonane (as internal standard for GC). The flask was degassed with argon and placed into a constant temperature bath at 90 °C. After the mixture was stirred vigorously for 5 min, 4-methylbenzyl alcohol (1 mmol) was added to it, and the reaction was allowed to continue at 90 °C. Known volume of aliquots was withdrawn periodically, filtered through a short pad of celite, diluted with toluene and the organic layer was analyzed with GC against n-nonane as internal standard.

2.5. General procedure for the alkylation of arene with various benzylic alcohols using Ir/Sn catalyst (vide Section 3.1)

A 25 mL Schlenk flask equipped with a magnetic bar, was charged with [Ir(COD)(μ-Cl)]₂ (14 mg, 0.02 mmol), SnCl₄ (9.4 μL), arene (37.6 mmol) and n-nonane (as internal standard for GC). The flask was degassed with argon and placed into a constant temperature bath at 90 °C. After the mixture was stirred vigorously for 5 min, the corresponding alcohol (2 mmol) was added to it, and the reaction was allowed to continue at 90 °C. The mixture was analyzed by GC (as described previously) to determine the yield and conversion. For isolation of the products, the mixture was quenched with aqueous NH₄F solution and extracted with diethyl ether (4 × 25 mL). The combined extract was washed with water (2 × 10 mL), brine (2 × 10 mL), dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The product was purified by column chromatography (Silica gel 100/200 mesh, eluent:pet ether, or EtOAc/pet ether 1:9 (v/v).

2.6. General procedure for competitive benzylation kinetics (vide Sections 3.5 and 3.6)

A 25-mL Schlenk flask equipped with a magnetic bar, was charged with [Ir(COD)(μ-Cl)]₂ (7 mg, 0.01 mmol), SnCl₄ (5.8 μL, 0.04 mmol), benzene (10 mmol), toluene (10 mmol), and n-nonane (as internal standard for GC). The flask was degassed with argon and placed into a constant temperature bath at 90 °C. After the mixture was stirred vigorously for 5 min, the corresponding benzyl alcohol (1 mmol) was added to it, and the reaction was allowed to continue at 90 °C for additional 20 min. Known volume of aliquots were withdrawn periodically, filtered through a short pad of celite, diluted with toluene and the organic layer was analyzed with GC against n-nonane as internal standard. Average k_T/k_B value was determined from 5-sets of data collected within a span of 20 min. The o:m:p ratio was determined at the end of the reaction.

2.7. General procedure non-competitive benzylation kinetics (vide Sections 3.3–3.8)

The procedure as in competitive benzylation (Section 2.6) was followed but with benzene or toluene (20 mmol) as the arene.

2.8. General procedure for Hammett studies (vide Section 3.4)

The procedure as in non-competitive benzylation kinetics studies (Section 2.7) was followed using the respective arenes and alcohols for each run. For Hammett study with respect to alcohol, the corresponding alcohol was varied in the reaction with toluene, and similarly for Hammett study with respect to arene, the respective aromatic partner was varied in the reaction with benzyl alcohol. Each kinetic experiment was performed three times for the determination of the rate constant values.

2.9. General procedure for kinetic isotope effect studies (vide Section 3.5)

Both competitive (Section 2.6) and non-competitive (Section 2.7) methods were followed for kinetic isotope effect studies using C₆H₆ and C₆D₆ as aromatic partners with benzyl alcohol (for non-competitive runs) or 4-methylbenzyl alcohol (for competitive runs) as the alkylating agent. Each kinetic experiment was performed three times for the determination of the rate constant values.

2.10. General procedure for the determination of activation parameters (vide Section 3.7)

The procedure as in non-competitive benzylation kinetics studies (Section 2.7) was followed for the reaction of 4-chlorobenzyl alcohol with toluene. The rate constant was
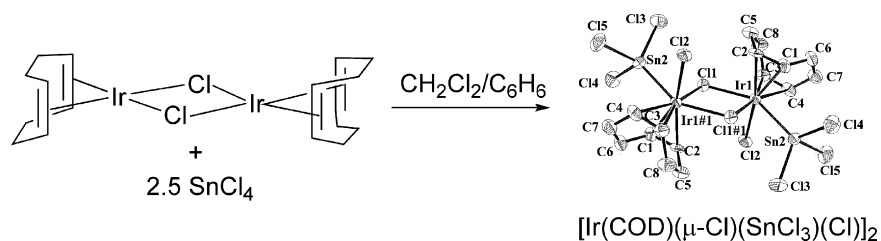
Scheme 1. Isolation of heterobimetallic complex [Ir^{III}(COD)(μ-Cl)(SnCl$_3$)Cl]$_2$ having Ir^{III}-Sn^{IV} core.

determined at the constant temperatures of 358, 368, 378 and 383 K. The temperature was maintained constant with a variation of ±0.1 °C using a Beckmann Mercury Contact Thermometer. Each kinetic experiment was performed three times for the determination of the rate constant values. Then from the Arhenious–Eyring plot, the activation parameters were determined.

2.11. Procedure for the study of the relative activity of the various Ir/Sn catalytic systems (A, B, C, D, E, F) (vide Section 3.8)

The yield of the reaction of toluene (20 mmol) with benzyl alcohol (1 mmol) at 90 °C was determined at different times following a similar method as described in non-competitive benzylation kinetics studies (Section 2.7). Each catalyst system (**A–F**) (0.01 mmol) was generated in situ by the reaction of the corresponding Ir(I) precursor complex and SnX$_4$. Each kinetic experiment was performed three times.

2.12. Procedure for IR studies with PhCN as probe (vide Section 3.8)

Stock solutions ($\sim 10^{-2}$ M) of SnX$_4$ (**I**), Ir(I) precursor complexes (**II**), and the IR probe PhCN (**III**) were prepared in dichloromethane at 300K. Samples for IR study were prepared by mixing **I**, **II**, and **III** in a molar ratio of 2:1:1 and then spreading a liquid film of the mixtures on KBr disc. To study the interaction of only SnX$_4$ with PhCN, samples were prepared by mixing **I** and **III** in 2:1 molar ratio. The reference blank spectrum for only PhCN was also obtained to compare the results.

3. Results and discussion

3.1. Reaction of arenes and heteroarenes with benzyl alcohols: Model study and scope

For model studies, we had chosen the benzylation of toluene with 4-methylbenzyl alcohol. A catalyst combination of 1 mol% [Ir(COD)(μ-Cl)]$_2$ and 4 mol% SnCl$_4$ (hereafter Ir/Sn catalyst) showed markedly superior activity at 90 °C affording 95% of ditolylmethane (o/p 17/83) just after 15 min and without any byproduct (Table 1, entry 1). The catalytic activity was undeterred even after six repetitive cycles without any loss of activity. Attempts were made to carry out the model reaction at lower temperatures than 90 °C, but the yields were drastically reduced (entries 3–5). It is noteworthy that the parent partners

Table 1
Model reaction of toluene with 4-methylbenzyl alcohol:catalyst screening[a]

Entry	Catalyst	Temperature (°C)	Time (min)	Yield[b] (%)
1	[Ir(COD)Cl]$_2$/4 SnCl$_4$	90	15	95 (87)
2		90	30	96 (89)
3		85	60	75
4		75	120	10
5		55	120	5
6	[Ir(COD)Cl]$_2$	90	360	0
7	SnCl$_4$	90	360	<1
8	IrCl$_3$	90	360	<1
9	IrCl$_3$ + 4 SnCl$_4$	90	360	2

[a] Rxn condition: toluene (18.8 mmol), 4-methylbenzyl alcohol (1 mmol), catalyst (0.01 mmol).
[b] Determined by GC, isolated yield in parentheses.

([Ir(COD)(μ-Cl)]$_2$ or SnCl$_4$) as well as a mere combination of IrCl$_3$ and SnCl$_4$ were ineffective (entries 6–9).

We have been also successful in isolating the heterobimetallic complex [Ir^{III}(COD)(μ-Cl)(SnCl$_3$)Cl]$_2$ from the reaction of [Ir(COD)(μ-Cl)]$_2$ and SnCl$_4$ (Scheme 1). The X-ray structure of the complex clearly established the presence of high-valent "Ir^{III}–Sn^{IV}" core.

Gratifyingly, as little as 1 mol% of the isolated high-valent complex [Ir^{III}(COD)(μ-Cl)(SnCl$_3$)Cl]$_2$ could promote the model alkylation reaction, affording 45% of ditolylmethane (o/p 19/81) after 6 h (Scheme 2). In contrast a low-valent Ir–Sn complex, namely [Ir^{I}(COD)SnCl$_3$] was inefficient. The above results augment our initial proposal, and suggest the superiority of the high-valent "Ir^{III}–Sn^{IV}" core in the present alkylation.

In our hand, the Ir/Sn reagent proved to be a very efficient catalyst for the alkylative coupling of arenes/heteroarenes with benzyl alcohols (Table 2). In all cases studied there has been 100% conversion of the starting benzyl alcohol, and the corresponding benzyl arenes were isolated with high selectivity
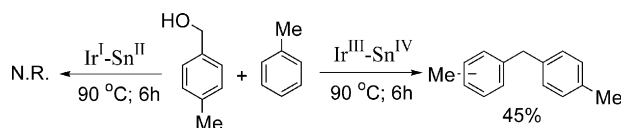
Scheme 2. Efficiency of high-valent Ir^{III}-Sn^{IV} vs. low-valent Ir^{I}-Sn^{II} in the benzylation of toluene (N.R. = no reaction).

Table 2
Ir/Sn catalyzed alkylation of arenes and heteroarenes with benzyl alcohols[a]
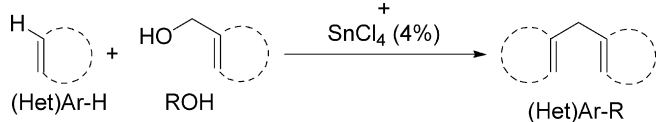
ArH= arenes; HetH= heteroarenes; R= 1° benzyl

#	ArH/HetH	ROH	Time (min)	Yield (%)[b]	Major product	Regioisomer
1	Benzene		30	70 (76)		–
2	Toluene		15	87 (95)		17:83 (o/p)
3	Toluene		30	86 (93)		38:62 (o/p)
4	o-Xylene		15	88 (96)		–
5	p-Xylene		15	95 (99)		–
6	Mesitylene		15	86		–
7	Ethylbenzene		20	88 (93)		30:5:65 (o/m/p)
8	Naphthalene		20	80		89:11 (o/p)
9	Bromobenzene		60	61 (65)		58:42 (o/p)
10	Anisole		5	87 (90)		66:34 (o/p)
11	Thiophene		15	95		67:33 (o/p)

[a] Rxn condition: ROH (1 mmol), ArH/HetH (20 mmol), [Ir(COD)(μ-Cl)]$_2$ (0.01 mmol), SnCl$_4$ (0.04 mmol), 90 °C.

[b] Isolated yield (GC yield in parentheses).

and in good to excellent yields. Presence of electron-donating groups in the arene/alcohol moiety enhanced the reaction rate, while electron-withdrawing groups caused longer reaction time. The reactions provided predominantly *ortho/para* substitution.

3.2. A working model on substrate activation and coupling across Ir/Sn catalyst

Inspired by the efficacy of the Ir/Sn catalyst, as well as the positive reactivity of the isolated Ir^{III}–Sn^{IV} complex we aimed at looking into the substrate activation and coupling in the alkylation reaction. Scheme 3 shows a working model, which is

based on our original catalyst design concept (vide Fig. 2). Here, the high-valent d^6-Ir^{III} center is regarded as electrophilic and a soft (or borderline) acid according to HSAB theory. Hence it is expected to have a strong affinity to electron-rich substrates such as arenes, which are also soft base [32–35]. Such a binding interaction is expected to be enhanced by the presence of strong π-acceptor SnCl$_3$$^-$ unit [36]. Simultaneously, the Lewis acidity of hard Sn^{IV} center is expected to activate the hard oxygen atom of benzyl alcohol [32–34]. The above synergistic activation might trigger the subsequent coupling reaction. To verify the above model we examined various parameters with the help of kinetic and spectroscopic studies. The key mechanistic questions that we aimed to answer are:
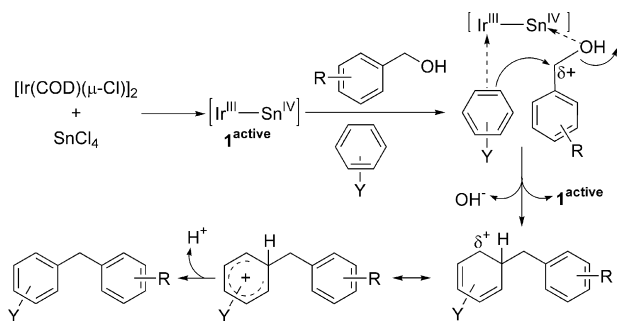
Scheme 3. A working model on substrate activation and coupling across Ir/Sn catalyst.

1. How does the alcohol get activated and whether the mechanism is electrophilic?
2. How does the aromatic ring participate in the reaction and whether the mechanism involves aromatic C–H activation?
3. Does the reaction resemble Friedel–Crafts like behavior?
4. How do the stereoelectronic properties across the two metals influence the catalytic efficiency and selectivity?

The results pertaining to the above inquiries are discussed in the following sections.

3.3. Catalyst–substrate interaction

To gain evidence on the proposed hard–hard activation of the electrophile at the tin center of the Ir/Sn catalyst, alkylation of toluene was performed with various benzylating agents such as acetate, ether, formate, and chloride. From the non-competitive rate constant measurement, the relative activity of the electrophiles has been evaluated. The results (Fig. 3) clearly show that the reactivity of the electrophiles decreases in the order OH > OAc > OMe > OC(O)H > Cl. This order can be roughly

correlated to the donor strength of the hard bases, and hence the strength of the "*tin–electrophile*" hard–hard interaction.

3.4. Hammett study with respect to alcohol and arene

To probe the nature of the transition state, the rate of the reaction of toluene with several *para*-substituted benzyl alcohols was measured leading to a linear free energy relationship between the relative rate constant (k_R/k_H) and the substituent constant (σ_p) (Fig. 4). The resulted negative Hammett reaction constant ρ value indicates an electrophilic mechanism for the present reaction. The moderate negative value indicates that the catalyst–substrate interaction leads to the generation of weak positive charge ($\delta+$) at the benzylic (–CH$_2$) carbon center of the alcohol (Fig. 4). Absence of a large negative reaction constant ρ value also indicates that in our system no "distinct free benzyl cation" is being formed [37].

Hammett study was also carried out by varying the substituents at the aromatic ring. The rate constants (k_X) at 90 °C were determined for the reaction of benzyl alcohol with various aromatic substrates with varying X group, and the corresponding Hammett plot was obtained (Fig. 5). In the present study, two types of linear plots with different ρ value were obtained. For the electron-donating substituents (EDG) the observed ρ value was more negative (−4.34), as compared to the ρ value (−1.15) obtained for the electron-withdrawing substituents (EWG). The data indeed indicates an electrophilic mechanism but offers a
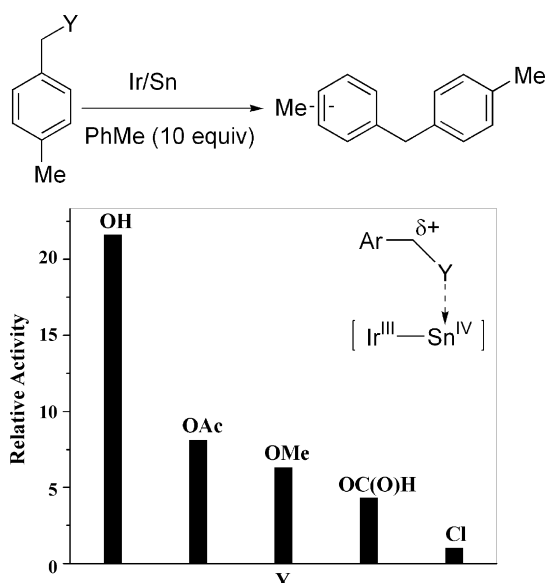

Fig. 3. Variation of alkylation rate for benzylic substrates PhCH$_2$-Y against HSAB donor strength of Y indicating Sn···Y hard–hard interaction.
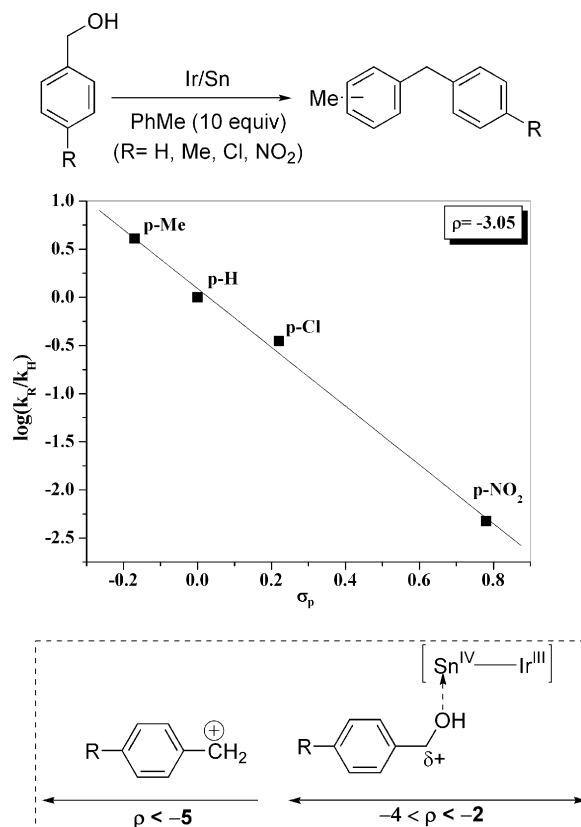

Fig. 4. Hammett plot with respect to alcohols in Ir/Sn catalyzed alkylation, suggesting the absence of free benzyl cation in T.S.
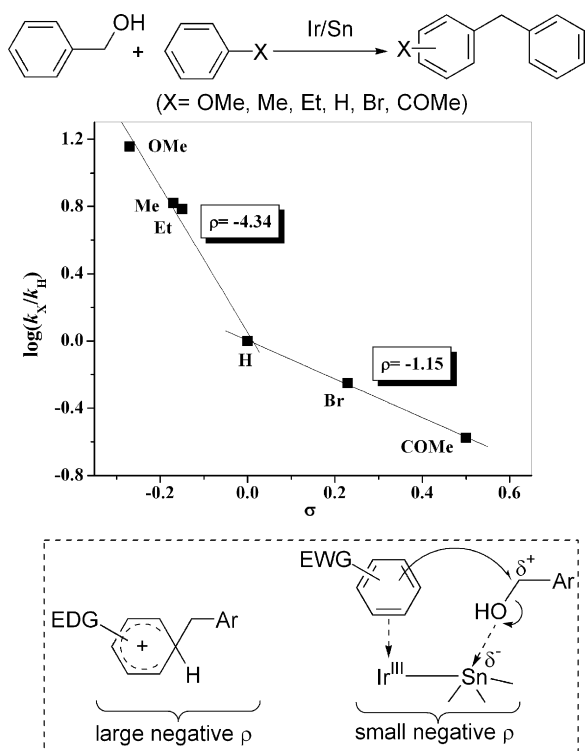
Fig. 5. Hammett Plot with respect to arene in Ir/Sn catalyzed alkylation, suggesting T.S. variation with respect to substitutent (EDG, and EWG).

Table 3
Non-competitive and competitive rate constants for the alkylation of benzene and benzene-d_6

Non-competitive			Competitive		
ArH	$k \times 10^4$ (s^{-1})	k_H/k_D	k_T/k_D	k_T/k_H	k_H/k_D
C_6H_6	3.2	1.14	18.3	16.8	1.09
C_6D_6	2.8				

itive and non-competitive benzylation kinetics are presented in Tables 4 and 5. The noteworthy points are:

(i) that the reactions give predominantly *ortho–para* substitution,
(ii) that k_T/k_B ratios are similar in competitive and non-competitive runs,
(iii) that competitive k_T/k_B ratio and isomer distribution are independent of time within a span of 1–20 min,
(iv) that electron-donating Me substituent in the benzyl alcohol increases the k_T/k_B ratio but lowers the *ortho/para* ratio.

The above results point towards a Friedel–Crafts like behavior of the present reaction.

3.7. Determination of activation parameters

We have briefly examined the activation parameters in the Ir/Sn catalyzed alkylation reaction. The rate of the Ir/Sn catalyzed reaction of toluene with 4-chlorobenzyl alcohol was measured at different temperatures from 358 K to 383 K. From the corresponding Arrhenius–Eyring plot, the activation parameters were determined (Table 6, Fig. 7). The reaction is

difference in behavior from typical electrophilic aromatic substitution reaction where the values are usually in the range −5 to −9 [37–39]. The observed difference in ρ values might be due to difference in transition state structures, and a mere speculation is shown in Fig. 5.

3.5. Kinetic isotope effect

To elucidate whether aromatic C–H activation is involved in the Ir/Sn catalyzed alkylation reaction, the kinetic isotope effect was studied. If C–H activation path is involved a substantial primary kinetic isotope effect would be expected.

The competitive benzylation of toluene/benzene and toluene/benzene-d6 mixture with 4-methylbenzyl alcohol was carried out in presence of catalytic Ir/Sn at 90 °C. The non-competitive benzylation of benzene and benzene-d6 with benzyl alcohol was also performed and the non-competitive rate constant values were determined. Results from both the studies are summarized in Table 3 and Fig. 6. The observed very small secondary kinetic isotope effect rules out an arene C–H bond activation, and suggests that the activated state is closer in nature to an oriented π-complex [37–41].
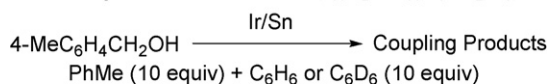
3.6. Competitive and non-competitive rate studies: substrate and positional selectivities

We also felt appropriate to carry out some competitive and non-competitive benzylation kinetics to evaluate whether the present reaction follows typical Friedel–Crafts like pattern [42]. The experimental results of the comparative studies on compet-
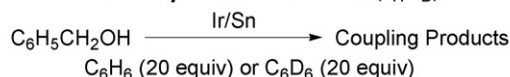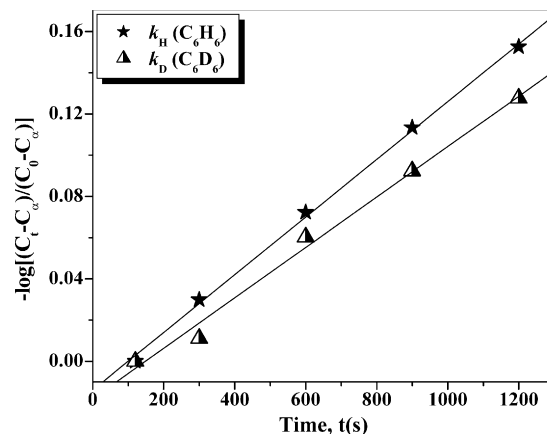

Fig. 6. Rate plots in the Ir/Sn catalyzed alkylation of C_6H_6 and C_6D_6 with benzyl alcohol.

Table 4

Substrate (k_T/k_B) and positional selectivity (*o:m:p*) for Ir/Sn catalyzed reaction of benzene/toluene with 4-substituted benzyl alcohols

R	Non-competitive				Competitive	
	$k_T \times 10^4$ (s^{-1})	$k_B \times 10^4$ (s^{-1})	k_T/k_B	*o:m:p*	k_T/k_B	*o:m:p*
H	21.1	3.2	6.6	37:5:58	6.0	44:4:52
p-CH$_3$	86.1	4.2	20.5	33:0:67	16.8	38:0:62
p-Cl	7.4	1.6	4.6	51:0:49	5.6	52:0:48

Table 5

Effect of reaction time on substrate (k_T/k_B) and positional selectivity (*o:m:p*) for Ir/Sn catalyzed reaction of benzene/toluene with 4-substituted benzyl alcohols

Time (min)	R					
	H		Me		Cl	
	k_T/k_B	*o:m:p*	k_T/k_B	*o:m:p*	k_T/k_B	*o:m:p*
02	5.95	36:5:59	16.89	35:0:65	5.96	50:2:48
05	5.90	37:5:58	16.76	34:0:66	5.13	50:2:48
10	5.91	37:6:57	16.86	34:0:66	5.54	51:2:47
15	5.95	38:5:57	16.84	34:0:66	5.62	51:<1:49
20	6.04	37:5:58	16.82	33:0:67	5.80	51:0:49

characterized by a positive enthalpy of activation, and small negative entropy of activation [37–41].

3.8. Effect of electronic tuning around Ir/Sn on the catalyst reactivity

According to our original proposal (vide Fig. 2), one can tune the stereoelectronic parameters at both the metal centers in Ir^{III}-Sn^{IV} core by changing the ligand appendage. To see whether such change can modulate the catalytic activity, we undertook the following study.

Table 6

Activation parameters in Ir/Sn catalyzed reaction of toluene with 4-chlorobenzyl alcohol

Temperature (K)	$k \times 10^4$ (s^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (J K^{-1} mol^{-1})
358	2.242	105.1	−21.7
368	8.268		
378	16.459		
383	25.552		

3.8.1. Tuning around iridium

The diene ligand in the precursor iridium complex was changed from 1,5-cyclooctadiene (COD), to 2,5-norbornadiene (NBD) and 1,3-cyclohexadiene (CHD), and the alkylation reaction was carried out with the corresponding Ir/Sn complexes. The resulting relative catalytic efficiency was found to be in the order "Ir-COD" (**A**) > "Ir-NBD" (**B**) > "Ir-CHD" (**C**) (Fig. 8).

The effect of the change of the attached diene ligand was again evaluated via a parallel experiment with the help of IR spectroscopy. Thus the order of complexing ability of the corresponding complexes with the IR probe molecule PhCN was measured by monitoring the change in the CN stretching frequency, $\Delta\nu_{CN}$ [$\Delta\nu_{CN} = \nu$(complex + PhCN) − ν(free PhCN)]. It was observed in the same order as the catalytic activity of the complexes (Fig. 8).

Therefore, from this particular experiment we can conclude that the variation of the attached diene ligand changes the stereoelectronic parameter at the central iridium atom and thus changes the electrophilic strength of the complexes as reflected by the change of catalytic activity and the strength of Lewis acidity ($\Delta\nu_{CN}$).
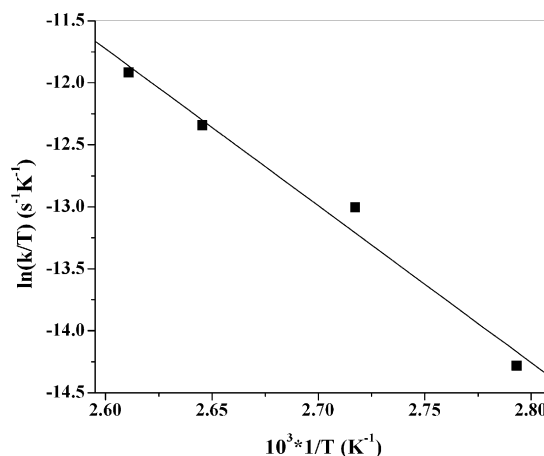

Fig. 7. Arrhenius–Eyring plot in Ir/Sn catalyzed reaction of toluene with 4-chlorobenzyl alcohol.
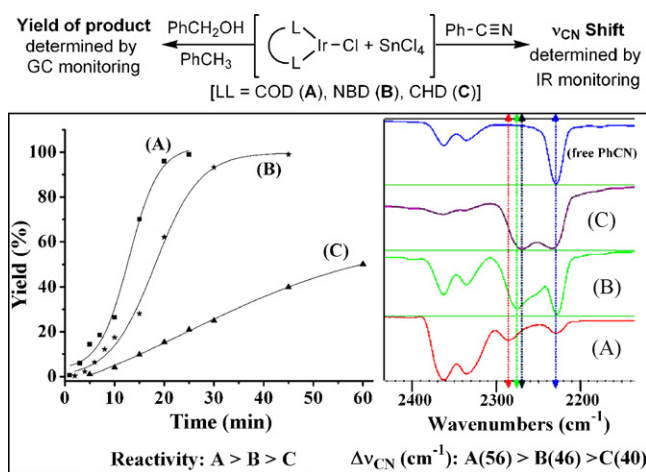
Fig. 8. Electronic tuning at Ir-center vs. catalytic efficiency: (left) rate-profile; (right) IR-shift of PhCN probe.
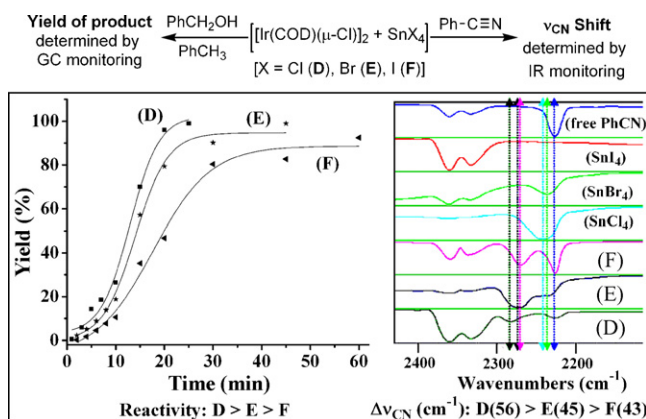

Fig. 9. Electronic tuning at Sn-center vs. catalytic efficiency: (left) rate-profile; (right) IR-shift of PhCN probe.

3.9. Tuning around tin

The hard-hard interaction between the Lewis acidic Sn(IV) center and the oxygen atom of the alcohol molecule can be considered as another important factor in this reaction. To examine the effect of the change in Lewis acidity at the tin center, the halogen atom (X) in SnX_4 was changed from Cl to Br and I (Fig. 9).

The extent of the Lewis acidic strength was measured by a similar IR experiment taking PhCN as the probe. The shift ($\Delta\nu$) was found to be in the order "Ir/SnCl$_4$" (**D**) > "Ir/SnBr$_4$" (**E**) > "Ir/SnI$_4$" (**F**). Most interestingly, the rate of the benzylation of toluene with benzyl alcohol was also observed to be in the same order (Fig. 9). Thus we can say that a change in Lewis acidity at the tin center of the bimetallic catalyst has a pronounced effect in the catalytic efficiency as reflected by the rate profile and the IR shift $\Delta\nu_{CN}$.

4. Summary and conclusion

In summary we have demonstrated the profound catalytic reactivity of the dual-reagent [Ir(COD)(μ-Cl)]$_2$/SnCl$_4$ catalyst

towards the alkylative coupling of arene/heteroarene with benzyl alcohols. We have been also successful in isolating a hetero-bimetallic complex namely [Ir^{III}(COD)(μ-Cl)(SnCl$_3$)Cl]$_2$ from the reaction of [Ir(COD)(μ-Cl)]$_2$ and SnCl$_4$. This isolated catalyst bears a high-valent Ir^{III}-Sn^{IV} core, and is effective in promoting the alkylation reaction at only 1 mol% catalyst loading. We have further tested the validity of a working model that invokes (a) activation of alcohol (a hard donor) at the hard Sn^{IV}-center, and (b) activation of arene at the soft Ir^{III}-center. The following evidences have been presented in support of the above model.

(a) The alkylation rate for benzylic substrates PhCH$_2$-Y varied according to the HSAB donor strength of Y in the order OH > OAc > OMe > OC(O)H > Cl suggesting the role of the "*tin–electrophile*" hard–hard interaction.
(b) A negative Hammett reaction constant ρ value (-3.05) was obtained with respect to benzyl alcohol, which indicates an electrophilic mechanism with the generation of weak positive charge ($\delta+$) at the benzylic (–CH$_2$) carbon center of the alcohol.
(c) Hammett study with respect to arene showed negative Hammett reaction constant ρ values (-4.34 for EDG, and -1.15 for EWG), while kinetic isotope effect study indicated a k_H/k_D value of 1.09–1.14. These results disfavor a C–H activation pathway and support an electrophilic aromatic substitution reaction. Interestingly, the competitive and non-competitive rate studies (isomer distribution and k_T/k_B ratio) showed a similarity with Friedel–Crafts like kinetics. Temperature dependent kinetics showed that the reaction is characterized by a positive enthalpy of activation, and small negative entropy of activation.

Finally, we have also demonstrated that the catalytic efficiency can be tuned by varying the diene ligand around the iridium center, or the halogen atom around the tin center. This could serve as a guide to further improve the efficacy of the Ir/Sn catalysts.

References

[1] E.K. van den Beuken, B.L. Feringa, Tetrahedron 54 (1998) 12985.
[2] M. Shibasaki, in: F. Vögtle, J.F. Stoddart, M. Shibasaki (Eds.), Stimulating Concepts in Chemistry, Wiley-VCH, Weinheim, 2000, pp. 105–121.
[3] N. Wheatley, P. Kalck, Chem. Rev. 99 (1999) 3379.
[4] D.E. Fogg, E.N. dos Santos, Coord. Chem. Rev. 248 (2004) 2365.
[5] S. Kamijo, Y. Yamamoto, in: M. Shibasaki, Y. Yamamoto (Eds.), Multimetallic Catalysts in Organic Synthesis, Wiley-VCH, Weinheim, 2004, pp. 1–52.
[6] G.J. Rowlands, Tetrahedron 57 (2001) 1865.
[7] J.-A. Ma, D. Cahard, Angew. Chem. Int. Ed. 43 (2004) 4566.
[8] J. Choudhury, S. Podder, S. Roy, J. Am. Chem. Soc. 127 (2005) 6162.
[9] S. Podder, J. Choudhury, S. Roy, J. Org. Chem. 72 (2007) 3129.

[10] S. Podder, J. Choudhury, U.K. Roy, S. Roy, J. Org. Chem. 72 (2007) 3100.
[11] U.K. Roy, P.K. Jana, S. Roy, Tetrahedron Lett. 48 (2007) 1183.
[12] U.K. Roy, S. Roy, Tetrahedron 62 (2006) 678.
[13] U.K. Roy, S. Roy, J. Organomet. Chem. 691 (2006) 1525.
[14] M. Banerjee, S. Roy, J. Mol. Catal. A 246 (2006) 231.
[15] M. Banerjee, U.K. Roy, P. Sinha, S. Roy, J. Organomet. Chem. 690 (2005) 1422.
[16] M. Banerjee, S. Roy, Org. Lett. 6 (2004) 3137.
[17] P. Sinha, S. Roy, Organometallics 23 (2004) 67.
[18] M. Banerjee, S. Roy, Chem. Commun. (2003) 534.
[19] P. Sinha, S. Roy, Chem. Commun. (2001) 1798.
[20] A. Kundu, S. Prabhakar, M. Vairamani, S. Roy, Organometallics 18 (1999) 2782.
[21] A. Kundu, S. Prabhakar, M. Vairamani, S. Roy, Organometallics 16 (1997) 4796.
[22] G.A. Olah, Friedel–Crafts and Related Reactions, vol. II, Wiley-Interscience, New York, 1964, part 1.
[23] G.A. Olah, A Life of Magic Chemistry. Autobiographical Reflections of a Nobel Prize Winner, Wiley-Interscience, New York, 2001.
[24] R.M. Roberts, A.A. Khalaf, Friedel–Crafts Alkylation Chemistry. A Century of Discovery, Marcel Dekker, New York, 1984.
[25] G.A. Olah, J. Org. Chem. 66 (2001) 5943.
[26] M. Bandini, A. Melloni, A. Umani-Ronchi, Angew. Chem. Int. Ed. 43 (2004) 550.
[27] G. Brauer (Ed.), Handbook of Preparative Inorganic Chemistry, vol. 1, second ed., Academic Press, London, 1963.
[28] R. Walter, S. Kirchner, R. Franz, U.S. Patent (2002), 6399804.
[29] S.A. Bezman, P.H. Bird, A.R. Fraser, J.A. Osborn, Inorg. Chem. 19 (1980) 3755.
[30] G. Winkhaus, H. Singer, Chem. Ber. 99 (1966) 3610.
[31] J.F. Young, R.D. Gillard, G. Wilkinson, J. Chem. Soc. (1964) 5176.
[32] R.G. Pearson, Hard and Soft Acids and Bases, DOWDEN, Stroudsburg, 1973.
[33] R.G. Pearson, Chemical Hardness, Wiley-VCH, Weinheim, 1997.
[34] S. Woodward, Tetrahedron 58 (2002) 1017.
[35] M. Janka, W. He, A.J. Frontier, C. Flaschenriem, R. Eisenberg, Tetrahedron 61 (2005) 6193, and references therein.
[36] M.S. Holt, W.L. Wilson, J.H. Nelson, Chem. Rev. 89 (1989) 11.
[37] J. Clayden, N. Greeves, S. Warren, P. Wothers, Organic Chemistry, Oxford Univ. Press, New York, 2001.
[38] P. Sykes, A Guidebook to Mechanism in Organic Chemistry, sixth ed., Pearson Education Inc., Singapore, 1986.
[39] J. March, Advanced Organic Chemistry, Reactions, Mechanisms, and Structure, fourth ed., Wiley-Interscience, New York, 1992.
[40] A.A. Frost, R.G. Pearson, Kinetics and Mechanism. A Study of Homogeneous Chemical Reactions, Wiley Int. Ed., New York, 1961.
[41] K.J. Laidler, Chemical Kinetics, third ed., Pearson Education Inc., Singapore, 1987.
[42] G.A. Olah, S. Kobayashi, M. Tashiro, J. Am. Chem. Soc. 94 (1972) 7448.