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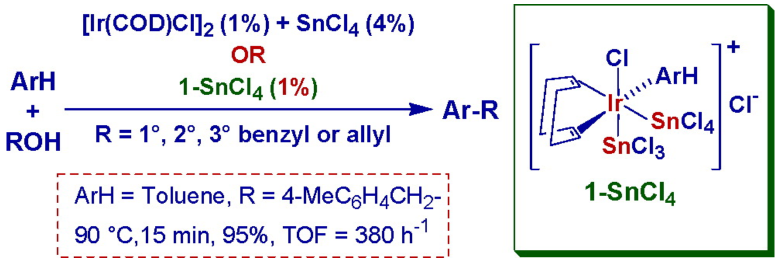

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Cooperative Friedel−Crafts Catalysis in Heterobimetallic Regime: Alkylation of Aromatics by π-Activated Alcohols

Joyanta Choudhury, Susmita Podder, and Sujit Roy*

Organometallics & Catalysis Laboratory, Chemistry Department, Indian Institute of Technology, Kharagpur 721302, India

Received January 29, 2005; E-mail: sroy@chem.iitkgp.ernet.in

By virtue of its astonishing success with regard to versatility, scope, and applicability, Friedel−Crafts alkylation reaction (hereafter FCA) continues to attract synthetic chemists to further enrich a knowledge base of more than 125 years.[1] The history of FCA catalysts witnessed many landmarks in both homogeneous and heterogeneous regimes. In the former case, transition metal halides are long established as FCA catalysts. On the contrary, catalysts bearing a high-valent Lewis acidic transition metal core, which are so well adapted for many organic reactions,[2] remain very little explored toward FCA.[3] In the course of our continuing effort to exploit the organic reactivity of a reagent combination involving transition metal and tin as partners,[4] we became attracted to the recent heightened interest in cooperative catalysis in heterobimetallic regime.[5] In practice, two design features exemplify such a 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. Irrespective of their types, heterobimetallic catalysts offer superior results in terms of efficiency and selectivity relative to the individuals. Within an $Ir^{III}-Sn^{IV}$ framework, we report here both type-I and apparent type-II catalysts, which promote FCA of arene using π-activated 1, 2, and 3° alcohols at very high efficiency.

The discrete heterobimetallic homogeneous type-I catalyst, namely, $[Ir_2(COD)_2(SnCl_3)_2Cl_2(\mu\text{-}Cl)_2]$ **1**, was easily synthesized via the oxidative addition reaction of $SnCl_4$ across $[Ir(COD)Cl]_2$ **2** in benzene−methylene chloride and slow crystallization. A more efficient apparent type-II catalyst (**1-SnCl$_4$**) was generated by mixing **1** and $SnCl_4$ in a 1:2 molar ratio at 90 °C. It can also be generated in situ by simply mixing **2** and $SnCl_4$ in a 1:4 molar ratio at 90 °C. The crystal structure of **1** confirms a cis-addition of Sn−Cl across iridium and retention of the halobridge as in the iridium precursor (Figure 1). The presence of the discrete $Ir^{III}-Sn^{IV}$ unit in **1** is noteworthy. In post-analysis, we reckon that the high-valent "Ir−Sn" core might be responsible for the superior electrophilicity and observed FCA reactivity in our case.

Olah, in a seminal paper, classified 127 FCA catalysts based on their activity in benzylation reactions; $SnCl_4$ is placed in a *weak group* (very low TOF), while $IrCl_3$ is placed in *very weak group* (<1% yield).[6,7] We reasoned that a high-valent "Tm−Sn" core (Tm is Ir here) is well poised to test the principle of cooperativity originating from the interplay of π-acidity/weak π-basicity at the Tm center, electrophilicity at the Sn center, and a metal−metal bond. Would cooperativity impart high Lewis acidity in such a core—an essential criterion for a successful FCA-catalyst? To test this hypothesis, we selected the FCA of aromatics with benzyl alcohol as the alkylating agent. This classical and industrially useful FCA process has been studied with traditional FC catalysts, lanthanide/actinide triflates, $H_2PtCl_6{\cdot}6H_2O$, modified clays, and Nafion-H, at 10−120% loading and a temperature of 80−120 °C.[7,8]

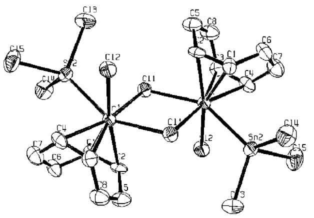

Figure 1. ORTEP diagram of **1** with 50% probability thermal ellipsoids.

Table 1. FCA of Toluene with 4-Methylbenzyl Alcohol[a]

entry	catalyst	time (min)	TOF (h^{-1})	yield (%)[b]
1	$SnCl_4$	360	<0.2	<1
2	$IrCl_3$	360	<0.2	<1
3	$IrCl_3 + 4SnCl_4$	360	0.3	2
4	$[Ir(COD)Cl]_2$ **2**	360	0	0
5	$[Ir_2(COD)_2(SnCl_3)_2Cl_2(\mu\text{-}Cl)_2]$ **1**	15	40	10
6		360	7.5	45 (36)[c]
7	**1-SnCl$_4$**[d]	15	324	81 (75)
8		30	190	95 (84)
9	**1-SnCl$_4$**[e]	15	380	95 (87)
10		30	192	96 (89)
11	$Sc(OTf)_3$	15	8	2
12[f]		360	5	30 (29)

[a] Conditions: toluene (18.8 mmol), alcohol (1 mmol), catalyst (0.01 mmol), T = 90 °C. [b] Determined by GC, isolated yield in parentheses. [c] Along with 26% *p*-tolualdehyde. [d] As benzene adduct. [e] Generated in situ from **2**. [f] With 0.05 mmol $Sc(OTf)_3$ as catalyst.

Model study on the benzylation of toluene with 4-methylbenzyl alcohol at 90 °C shows that as little as 1 mol % of catalyst **1** can promote FCA, affording 45% of ditolylmethane (o/p 19/81) after 6 h (Table 1, entry 6). Under similar conditions, even 5 mol % scandium triflate afforded only 30% of the alkylated product (entry 12). It is noteworthy that a mere combination of $IrCl_3$ and $SnCl_4$ is ineffective (entry 3), suggesting the importance of the high-valent "Ir−Sn" core. The apparent type-2 catalyst, **1-SnCl$_4$**, shows markedly superior catalytic activity affording 81−95% of product (o/p 17/83) just after 15 min without any byproduct (entries 7 and 9). The catalytic activity was undeterred even after six repetitive cycles without any loss in TOF.

The above results prompted us further to test whether cooperative activation of iridium can be done by other FCA catalysts. Accordingly, benzylation of toluene was carried out with a dual-catalyst combination of $[Ir(COD)Cl]_2$ **2** (1 mol %) and a FCA catalyst (4 mol %), representing each of the four groups in Olah's seminal paper. Surprisingly, all of the combinations tested with $AlCl_3$, $Sc(OTf)_3$, $InCl_3$, $TiCl_4$, and $ZnCl_2$ failed highlighting the importance of the "Ir−Sn" core (Supporting Information, Table S1).

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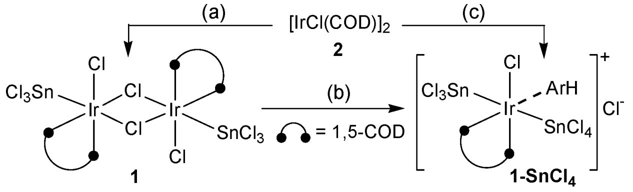
Table 2. Competitive and Noncompetitive Benzylation of Toluene and Benzene with Substituted Benzyl Alcohol 4-RC_6H_4-CH_2OH

		Competitive		Noncompetitive				
entry	R	k_T/k_B	o:m:p	$k_T \times 10^4$ (s^{-1})	$k_B \times 10^4$ (s^{-1})	k_T/k_B	k_R/k_H	σ_p^+
1	H	6.0	37:5:58	21.1	3.2	6.6	1	0
2	Me	16.8	33:0:67	86.1	4.2	20.5	1.3	−0.17
3	Cl	5.6	51:0:49	7.4	1.6	4.6	0.5	0.23

Scheme 1 [a]



[a] (a) 2 equiv of $SnCl_4$, $CH_2Cl_2-C_6H_6$, RT; (b) 2 equiv of $SnCl_4$, ArH, 90 °C; (c) 4 equiv of $SnCl_4$, ArH, 90 °C.

An obvious question at this stage is which other "Tm−Sn" motif can show promising FCA activity. Catalyst screening with a dual-catalyst combination of $SnCl_4$ (4 mol %) and a Tm partner (1 mol %) shows that $CoCl(PPh_3)_3$, $RuCl_2(PPh_3)_3$, and $NiCl_2(PPh_3)_2$ are inactive, while $PdCl_2(PPh_3)_2$ and $PtCl_2(PPh_3)_2$ are very weakly active (up to 5% FCA product). Promising activity is shown by $RhCl(PPh_3)_3$ and $RhCl(CO)(PPh_3)_2$, but TOFs are much lower compared to those in "Ir−Sn" catalysts discussed earlier (Supporting Information, Table S2).

In the context of the present investigation, it must be emphasized that although the organic reactivity of catalytic Ir(I) complexes is so well established, that of catalytic Ir(III) is only beginning to emerge.[9,10] The latter includes LA-type catalysis, catalytic C−H activation, and cycles involving Ir(III)/Ir(I) or Ir(III)/Ir(IV). Interestingly, for olefin arylation, Periana showed a non-FC C−H activation pathway.[10] In view of the above, we felt it appropriate to carry out preliminary kinetic studies to evaluate whether the present reaction follows FCA pattern.[6a] The data for competitive and noncompetitive benzylation reactions of toluene and benzene with para-substituted benzyl alcohols using in situ generated **1-SnCl$_4$** as catalyst at 90 °C indeed show familiar FCA behavior (Table 2, and Supporting Information, Tables S3 and S4). The noteworthy points are (1) that the reactions give predominantly ortho-para-substitution, (2) that k_T/k_B ratios are similar in competitive and noncompetitive runs, (3) that competitive k_T/k_B ratio and isomer distribution are independent of time within a span of 1−20 min, (4) that electron donating Me substituent in the benzyl alcohol increases the k_T/k_B ratio but lowers the ortho/para ratio,[6a] and (5) that the $\log(k_R/k_H)$ values linearly correlate with Hammett σ_p^+ constants.

The apparent type-II catalyst was isolated as a benzene adduct (**1-SnCl$_4$·PhH**). The isolated adduct is highly moisture sensitive, soluble in benzyl alcohol, behaves as a 1:1 electrolyte in solution, and shows excellent FCA reactivity in the present benzylation reaction. From elemental analyses, conductivity measurement, FT-IR, Raman, TGA, NMR studies of the adduct, we conclude that the type-II catalyst (**1-SnCl$_4$**) is $[Ir(COD)(SnCl_3)Cl(SnCl_4)(arene)]^+Cl^-$ (Scheme 1 and Supporting Information).[11] This suggestion is further supported by an early work of Meyer on the existence of an "Ir−$SnCl_4$" donor−adduct isomer in $[Ir(SnCl_4)Cl(CO)(PPh_3)_2]$.[12] Attempts to grow crystals of **1-SnCl$_4$·ArH** for structure determination are underway.

The FCA reactivity of **1** and **1-SnCl$_4$** has been extended to various arenes, heteroarenes, and π-activated 1°/2°/3° alcohols (Supporting Information, Table S5). The distinct superiority of "$Ir^{III}-Sn^{IV}$" catalysts over homogeneous FCA catalysts is ascertained by lower catalyst loading, reduced reaction time, low alcohol:arene ratio, high conversion, and absence of byproduct(s). Spectroscopic and kinetic studies in line with the works of Olah, Shibasaki, and others are in progress to understand the role of the two cooperative metals.[13]

To our knowledge, this represents the first example of a cooperative FCA catalysis concept in heterobimetallic regime. Studies are underway to exploit the general applicability of the said concept and extend it further to enantioselective FCA.

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Supporting Information Available: Experimental procedures, spectral and analytical data, tables, and figures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) See Supporting Information for preliminary results.

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