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Platinum-Catalyzed C−H Arylation of Simple Arenes

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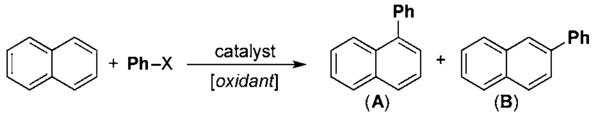
Supporting Information

ABSTRACT: This report describes the Na_2PtCl_4 catalyzed C−H arylation of arene substrates with diaryliodonium salts. The site selectivity of these reactions is predominantly controlled by steric factors. Remarkably, Na_2PtCl_4-catalyzed naphthalene arylation proceeds with opposite site selectivity compared to that obtained with Na_2PdCl_4 as the catalyst. Preliminary mechanistic studies provide evidence for a Pt^{II}/Pt^{IV} catalytic cycle involving rate-limiting C−C bond-forming reductive elimination.

Transition metal catalyzed C−H arylation reactions have emerged as valuable synthetic methods for the construction of biaryl linkages.[1] Over the past 15 years, there have been tremendous advances in this field, particularly in ligand-directed C−H arylation[2,3] and in the C−H arylation of heterocyclic scaffolds.[4] In contrast, the C−H arylation of simple aromatic substrates (lacking directing or activating groups) remains challenging.[3,5] While some high yielding transformations of this type have been developed,[6,7] it remains difficult to achieve high site selectivity as well as to predictably tune selectivity in these reactions.[8] These challenges are exemplified by the C−H arylation of the simple arene naphthalene, which can provide two isomeric products, **A** and **B**. As summarized in Table 1, most previously reported catalysts for this transformation provide modest selectivity for isomer **A**.

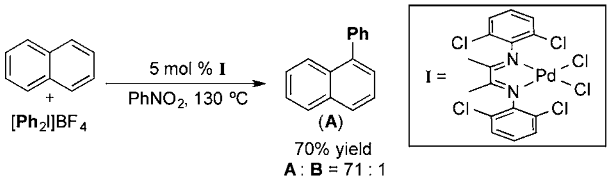
We recently demonstrated that diimine-ligated Pd catalyst **I** affords high selectivity for product **A** in the C−H arylation of naphthalene with $[Ph_2I]BF_4$ (70% yield, 71:1 ratio of **A** to **B**, eq 1).[16] This represents a promising example of catalyst-modulated selectivity in C−H arylation.[8] However, this method remains limited by a poor substrate scope (only naphthalene underwent high-yielding and site-selective C−H arylation). Furthermore, while highly **A**-selective catalysts have been identified, **B**-selectivity remains elusive in most of these transformations.

Table 1. Metal-Catalyzed C−H Arylation of Naphthalene



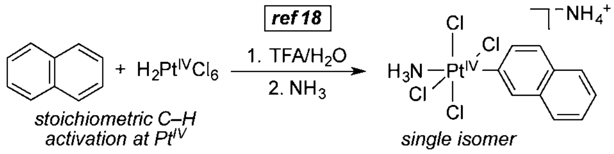
entry	Ph−X	catalyst	yield (%)	A:B
1[9]	PhH	$Pd(OAc)_2$	32[a]	>20:1
2[10]	$PhSnCl_3$	$PdCl_2$	40[a]	3.5:1
3[11]	$PhSiMe_3$	$PdCl_2$	38[a]	6.7:1
4[12]	PhI	$Pd(OAc)_2$	72[b]	3:1
5[13]	PhBr	Cp_2Ni	70[b]	2.3:1
6[14]	$[Ph_2I]BF_4$	Pd(II)@MOF-5(O_h)	64[b]	3:1
7[15]	$[Ph_2I]OTf$	$[Pd(OAc)(C{\sim}P)]_2$[c]	47[b]	1:1

[a] Based on naphthalene. [b] Based on Ph−X. [c] Herrmann-Beller catalyst; $(C{\sim}P) = CH_2C_6H_4P(o\text{-}Tol)_2$.



(1)

The mechanism of **I**-catalyzed naphthalene arylation with $[Ar_2I]BF_4$ is proposed to involve three key steps: (i) rate-limiting oxidation of Pd^{II} catalyst **I** to Pd^{IV} by $[Ph_2I]BF_4$, (ii) C−H activation of naphthalene at this Pd^{IV} intermediate, and (iii) C−C bond-forming reductive elimination from Pd^{IV} to release the biaryl product.[16] On the basis of this mechanism, we hypothesized that many of the prior limitations of this method could be addressed by changing the metal catalyst from Pd to Pt. Pt^{II} is generally easier to oxidize than Pd^{II},[17] which could potentially lead to an acceleration of the rate-limiting step of the catalytic cycle. Additionally, there is significant literature precedent for stoichiometric activation of electronically diverse arenes at Pt^{IV} centers (eq 2).[18] In these stoichiometric reactions, the selectivity of C−H cleavage is primarily dictated by steric factors, suggesting the feasibility of achieving high **B**-selectivity in Pt-catalyzed naphthalene arylation. However, a key challenge for this approach is that there are not, to our knowledge, any examples of Pt-catalyzed intermolecular C−H arylation in the literature[19] (in marked contrast to the hundreds of such transformations catalyzed by Pd).[1−5] This is likely due to the relatively high barrier for reductive elimination from Pt^{IV} compared to that from Pd^{IV}.[20]



(2)

We report herein the development of a new Pt-catalyzed C−H arylation of naphthalene and other simple arenes. Remarkably, a complete reversal in selectivity for naphthalene arylation is observed upon substituting Pt for Pd under

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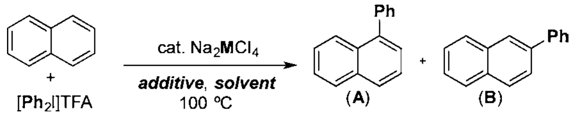
otherwise identical reaction conditions. Details on the scope and mechanism of this new transformation are presented.

Our initial studies focused on the C−H arylation of naphthalene with [Ph_2I]TFA (TFA = trifluoroacetate) catalyzed by Pd and Pt salts in trifluoroethanol (TFE) at 100 °C.[21] As anticipated based on our previous report,[16] the Pd catalyst Na_2PdCl_4 afforded the biaryl product with good selectivity for isomer **A** over **B** (Table 2, entry 1). However, remarkably, under otherwise identical conditions, changing the catalyst to the analogous platinum salt (Na_2PtCl_4) resulted in a complete reversal in selectivity (**A**:**B** = 1:10, entry 2). Optimization of the Pt-catalyzed reaction showed that the highest yields are obtained in neat naphthalene in the presence of 5 equiv of NBu_4OTf.[22] The Pt catalyst loading could be lowered to 2.5 mol %, and the product was obtained in 65% yield with 35:1 selectivity for isomer **B** (entry 4).

Table 2. Optimization of Naphthalene Phenylation

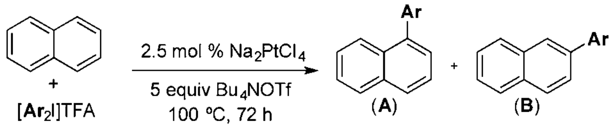


entry	[M]	solvent	additive	yield (%)[c]	A:B
1[a]	Pd	TFE	none	65	25:1
2[a]	Pt	TFE	none	31	1:10
3[a]	Pt	TFE	Bu_4NOTf	48	1:18
4[b]	Pt	none	Bu_4NOTf	65	1:35

[a]Conditions: [Ph_2I]TFA (1 equiv), naphthalene (30 equiv), [M] (10 mol %), additive (15 equiv), TFE (0.14 M), 100 °C, 24 h. [b]Conditions: [Ph_2I]TFA (1 equiv), naphthalene (60 equiv), Bu_4NOTf (5 equiv), [Pt] (2.5 mol %), 100 °C, 72 h. [c]GC yield.

This Pt-catalyzed reaction could be used to couple naphthalene with a variety of substituted aryliodonium salts. High **B**-selectivity (>20:1) was observed in all cases. Both electron-donating (Table 3, entries 1−3) and electron-withdrawing substituents (entries 4−7) on [Ar_2I]TFA were well-tolerated. A carbonyl-containing aryliodonium salt afforded a lower yield, possibly due to competing ligation and deactivation of the Pt-catalyst (entry 8). *Ortho*-substitution (as in [(*o*-tolyl)$_2$I]TFA) had a minimal deleterious effect on the yield (compare entries 2 and 3); however, the selectivity for isomer **B** was enhanced in this system (**A**:**B** < 1:100). This suggests that the Ar group may be ligated to Pt during the C−H cleavage step and that the steric environment at the Pt center could play a role in selectivity.

Table 3. Scope of [Ar_2I]TFA Reagents[a]

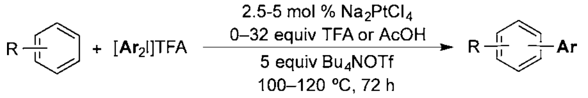


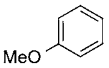
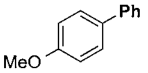
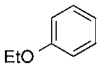
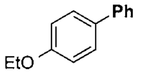
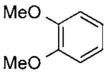
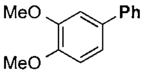
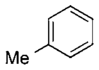
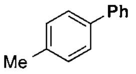
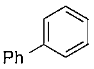
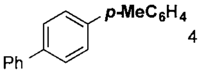
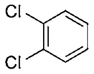
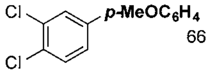
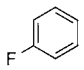
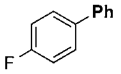
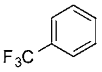
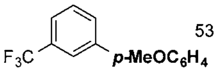
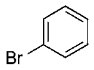
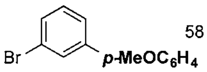
entry	Ar	yield (%)[b,c]	A:B[d]
1	*p*-$MeOC_6H_4$	84	1:25
2	*p*-MeC_6H_4	85	1:24
3	*o*-MeC_6H_4	72	>1:100
4	*p*-FC_6H_4	61	1:34
5	*p*-BrC_6H_4	57	1:27
6	*m*-BrC_6H_4	63	1:41
7	*p*-$CF_3C_6H_4$	53	1:30
8	*p*-AcC_6H_4	19	1:21

[a]Conditions: [Ar_2I]TFA (1 equiv), naphthalene (60 equiv), Na_2PtCl_4 (2.5 mol %), Bu_4NOTf (5 equiv), 100 °C, 72 h. [b]Isolated yield based on an average of two runs. [c]Mass balance is the corresponding Ar−Cl. [d]Ratio of isomers determined based on analysis of the crude reaction mixture by GC.

The scope of this transformation was next evaluated with respect to the arene coupling partner. As shown in Table 4, electronically diverse arenes participate in Pt-catalyzed C−H arylation with [Ar_2I]TFA. Steric factors dominate the site selectivity of these transformations.[7] Most notably, products of *ortho*-arylation are generally not detected in these systems. Additionally, disubstituted arenes react with high selectivity at the less hindered 4-position (entries 3 and 6).

Table 4. Scope of Arene Substrates[a]

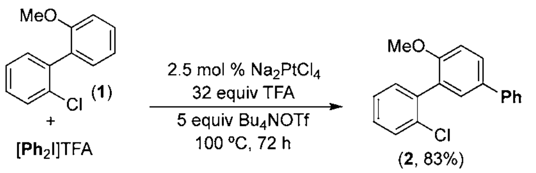


entry	substrate	major product	yield (%)[b,c]	selectivity[d]
1[f]			83	single isomer
2[f]			85	single isomer
3[f]			48	single isomer
4[e,f]			46	2.4 : 1 (*p* : *m*)
5[e]			42	1.2 : 1 (*p* : *m*)
6[g]			66	>20 : 1
7[e]			52	6 : 1 (*p* : *m*)
8[g]			53	1.4 : 1 (*m* : *p*)
9[g]			58	2.5 : 1 (*m* : *p*)

[a]Conditions: [Ar_2I]TFA (1 equiv), arene (30−60 equiv), Na_2PtCl_4 (2.5 mol %), Bu_4NOTf (5 equiv), TFA or AcOH (0 or 32 equiv), 100−120 °C, 72 h. [b]Isolated yield based on an average of two runs. [c]Mass balance is the corresponding Ar−Cl. [d]Ratio of isomers determined based on analysis of the crude reaction mixture by GC. [e]With 10 mol % Na_2PtCl_4. [f]With TFA. [g]With AcOH.

Electronic effects also play a role, particularly with monosubstituted arenes, where the *meta* and *para* sites are essentially sterically equivalent. With these substrates, modest to high selectivity is observed for reaction at the more electron rich of the two sites. For example, the best selectivities are obtained with anisole and ethoxybenzene (entries 1 and 2). In these cases, only products derived from *para*-arylation are detected. Electron-neutral arenes display modest selectivity for the *para* product over the *meta* product (entries 4 and 5). Finally, the inductively withdrawing trifluoromethyl substituent affords a slight preference for C−C bond formation at the *meta* site over the *para* position (*m*:*p* = 1.4:1, entry 8). Interestingly, the selectivity for C−H arylation of halide-substituted arenes varies with the halide (entries 6, 7, and 9).[23]

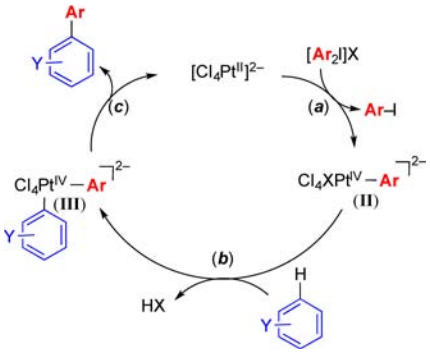
To probe the role of substrate electronics on the relative rates of these reactions, we conducted an intramolecular competition experiment (eq 3). Pt-catalyzed arylation of substrate **1** with $[Ph_2I]TFA$ proceeded with >100:1 selectivity on the more electron rich ring (*para* to the methoxy substituent), providing **2** as the only detectable product (83% yield). This result demonstrates that the reaction is significantly faster with electron rich arene substrates.

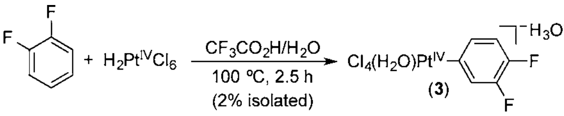


(3)

A plausible mechanism for this transformation is shown in Scheme 1 and is similar to that proposed for the related Pd-catalyzed transformation in eq 1.[16] To probe the viability of the first step (***a*** in Scheme 1) we examined the stoichiometric reaction between Na_2PtCl_4 and $[Ar_2I]TFA$ (Ar = 1,2-difluorophenyl). ^{19}F and ^{195}Pt NMR analysis showed the formation of a new Pt-aryl product after 8 min at 100 °C in anisole. This species has ^{19}F NMR resonances at −143.3 and −148.1 ppm, a ^{195}Pt NMR resonance at −724.8 ppm, and HRMS data consistent with a Pt^{IV} intermediate of general structure **II**.[24] However, this complex proved challenging to isolate. As a result, we pursued the synthesis of a close analogue of **II** using a modification of Shul'pin's procedure for stoichiometric C−H activation at $H_2Pt^{IV}Cl_6$.[18] The reaction of $H_2Pt^{IV}Cl_6$ with 1,2-difluorobenzene followed by purification via preparative TLC afforded the anionic aqua-Pt^{IV}Ar complex **3** (eq 4). Complex **3** was characterized by ^1H, ^{13}C, ^{19}F, and ^{195}Pt NMR spectroscopy, mass spectrometry, and elemental analysis. The ^{19}F NMR and ^{195}Pt NMR chemical shifts as well as the HRMS data for **3** are very similar (or identical) to those of the stoichiometric oxidation product **II** discussed above.

Scheme 1. Proposed Mechanism

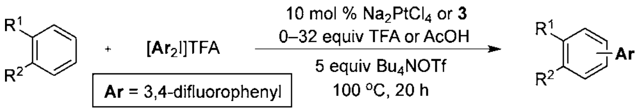


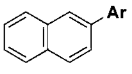
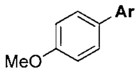


(4)

We further tested the ability of complex **3** to catalyze the arylation of a variety of substrates with $[Ar_2I]TFA$ (Ar = 1,2-difluorophenyl). Table 5 presents a comparison of this reaction to that catalyzed by the platinum salt Na_2PtCl_4 under identical conditions. In general, the two catalysts provided comparable yields and nearly identical selectivities for a range of C−H substrates (see Table S1 in the Supporting Information for additional examples). These results provide further support for the proposal that Pt^{IV}−aryl species **3**, or a close analogue thereof, is a likely intermediate in Na_2PtCl_4-catalyzed C−H arylation reactions.

Table 5. Comparison of C−H Arylation Catalyzed by Na_2PtCl_4 or 3[a]



entry	major product	yield (%) (Na_2PtCl_4)[b]	selectivity (Na_2PtCl_4)[c]	yield (%) (**3**)[b]	selectivity (**3**)[c]
1		56	20 :1	51	20 : 1
2[d,e]		47	single isomer	30	single isomer

[a]Conditions: $[Ar_2I]TFA$ (1 equiv), arene (30 or 60 equiv), TFA or AcOH (0 or 32 equiv), Na_2PtCl_4 or **3** (10 mol %), Bu_4NOTf (5 equiv), 100 °C, 20 h. [b]Yields determined by GC. [c]Ratio of products determined by GC. [d]With 30 equiv of arene. [e]With TFA.

With Pt^{IV} aryl complex **3** in hand as a close analogue of **II**, we investigated the final two steps of the proposed catalytic cycle (***b*** and ***c*** in Scheme 1). As anticipated, **3** (blue triangles in Figure 1) reacted with anisole over 6 h at 90 °C to form the biaryl product **5** (red diamonds in Figure 1). Furthermore, when this reaction was monitored by ^{19}F NMR spectroscopy, an intermediate (green circles in Figure 1) was observed to

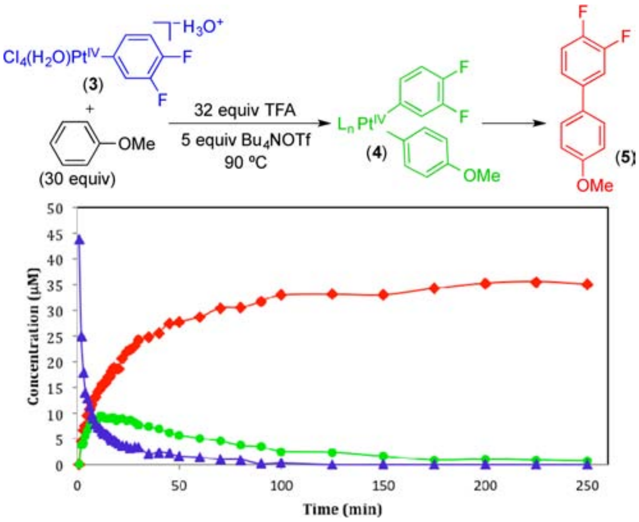


Figure 1. Reaction profile for the arylation of anisole with **3** (concentrations determined by ^{19}F NMR). ▲ = **3**; ◆ = **5**; ● = intermediate (proposed to be **4**).

form and then decay with the concomitant appearance of product **5**. We hypothesize that this intermediate may be a diaryl Pt^{IV} species (**4**, analogue of **III** in Scheme 1).[25] The observation of such an intermediate preliminarily suggests that reductive elimination is the rate-determining step in this Pt-catalyzed reaction.

We have conducted a number of additional studies to further probe the reaction mechanism. Rate studies show that both the C−H arylation of naphthalene and the C−H arylation of anisole are zero order in Ph_2I^+. Furthermore, comparison of the initial rate of naphthalene to that of naphthalene-d_8 show a k_H/k_D value of 1. An identical result was obtained with anisole/anisole-d_8. These data suggest that neither oxidation nor C−H cleavage is the rate-determining step of the catalytic reaction. This is consistent with the proposal (above) of C−C bond-forming reductive elimination as the rate-determining step.

In summary, this paper demonstrates the first example of intermolecular $Pt^{II/IV}$-catalyzed direct C−H arylation of simple arenes. The use of Na_2PtCl_4 in conjunction with diaryliodonium oxidants enables arylation of diverse substrates, with predominantly sterically controlled site selectivity. Preliminary mechanistic studies suggest that the transformation proceeds through a Pt^{II}/Pt^{IV} catalytic cycle and that reductive elimination may be rate limiting. Compared to analogous Pd-catalyzed arylation reactions (in which oxidation is rate limiting), the Pt-catalyzed conditions are effective for a much broader scope of substrates. Furthermore, the site selectivity of Pt-catalyzed naphthalene arylation is complementary to that observed with Pd catalysis. As such, this work represents an important step toward assembling a set of general, tunable catalysts for site-selective C−H functionalization of simple arenes.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete experimental and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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