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Rh(III)- and Ir(III)-Catalyzed C−H Alkynylation of Arenes under Chelation Assistance

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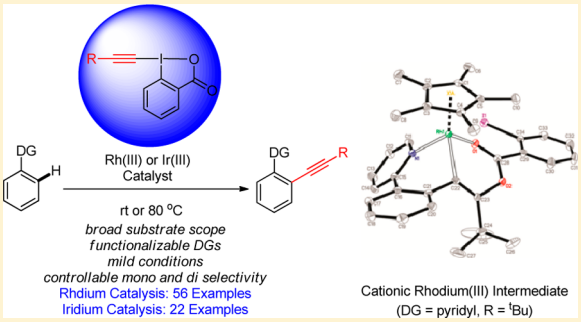
Supporting Information

ABSTRACT: An efficient Rh(III)- and Ir(III)-catalyzed, chelation-assisted C−H alkynylation of a broad scope of (hetero)arenes has been developed using hypervalent iodine-alkyne reagents. Heterocycles, *N*-methoxy imines, azomethine imines, secondary carboxamides, azo compounds, *N*-nitrosoamines, and nitrones are viable directing groups to entail *ortho* C−H alkynylation. The reaction proceeded under mild conditions and with controllable mono- and dialkynylation selectivity when both mono- and dialkynylation was observed. Rh(III) and Ir(III) catalysts exhibited complementary substrate scope in this reaction. The synthetic applications of the coupled products have been demonstrated in subsequent derivatization reactions. Some mechanistic studies have been conducted, and two Rh(III) complexes have been established as key reaction intermediates. The current C−H alkynylation system complements those previously reported under gold or palladium catalysis using hypervalent iodine reagents.



INTRODUCTION

Alkynes are fundamental building blocks in synthetic chemistry and in material science.[1] Although aryl alkynes are readily prepared from aryl halides by the Sonogashira reaction,[2] it is desirable and attractive to take advantage of the abundance of C−H bonds in arenes by a transition-metal-catalyzed C−H activation pathway. Indeed, this strategy has been increasingly explored in the past several decades, and a plethora of new synthetic methods have been developed toward the synthesis of complex structures.[3] Thus direct alkynylation of an aryl C−H bond would be highly desirable because the C−H bond is directly functionalized without preactivation, which is particularly important in the late stage functionalization of complex structures.

In contrast to the vast majority of C−H arylation reactions,[4] general methods of C−H alkynyation are limited that can be applied to a range of arenes with different electronic and steric characteristics. While it is desirable to apply terminal alkynes as alkynylating reagents via C−H/C−H oxidative coupling, only a narrow scope of heteroarenes such as thiophenes and highly electron-poor arenes such as pentafluorobenzene has been achieved.[5]

To achieve efficient C−H alkynylation, haloalkynes have been widely used.[6−8] In 2002, Yamaguchi reported the first example of C−H alkynylation of electron-rich arenes using chloroalkynes.[7] The C−H alkynylation of heterocycles was first reported by Gevorgyan using palladium catalysis.[8] In 2009 Chatani reported palladium catalyzed *ortho* alkynylation of acetanilide with bromoalkynes via a C−H activation pathway.[9] Recently, Chatani achieved the *ortho* C−H alkynylation of 2-phenylpyridines with haloalkynes in the presence of a stoichiometric amount of base.[6c] Despite the progress, the substrate scope remains limited.

To expand the substrate scope and to achieve C−H activation of intrinsically different arenes, alkynylated hypervalent iodines have been employed as a versatile and powerful alkynylating reagent.[10] In particular, as an oxidized and activated form of alkynes, 1-silylethynyl-1,2-benziodoxol-3(1H)-ones (silyl-EBXs) are readily synthesized in large scales in crystal forms and are stable toward air and moisture.[11] Since 2009 Waser and co-workers have elegantly and systematically applied EBXs to the electrophilic alkynylation of a range of heterocycles such as indoles, pyrroles, and furans using gold and palladium catalysts.[12] Copper catalysts may also effect alkynylation, as in Fujii and Ohno's reported coupling of bezamidines with EBXs,[13] but the relevancy of C−H activation remains mechanistically ambiguous. Thus when alkynylated hypervalent iodines are employed, the arene substrates are mostly limited to electron-rich (hetero)aromatics.[14] Given these limitations, it is necessary to develop a highly efficient and general alkynylation method for broadly defined arenes via a C−H activation pathway, particularly for generically and intrinsically less reactive ones.

It is well-known that installation of a directing group constitutes a common and effective strategy to entail C−H activation of intrinsically less reactive arenes.[3,4,15] In this context, C−H activation of arenes catalyzed by RhCp* and occasionally IrCp* complexes has garnered increasing attention.[15] However, Rh(III)-catalyzed C−H activation/C−C

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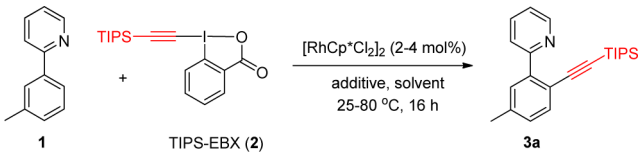
coupling is mostly limited to olefination, arylation, and redox-neutral insertion of the aryl C−H into a polar π bond,[16] and no Rh(III)-catalyzed C−H alkynylation of arenes has been reported. On the other hand, we[17a] and Su[17b] have recently reported the compatibility of Rh(III)-catalyzed C−H activation with hypervalent iodine oxidants as in efficient azidation, nitration, and amidation of arenes. We reasoned that hypervalent iodine-alkynes such as EBXs are desirable alkynylating reagents in rhodium(III)-catalyzed C−H activation. This is because, in addition to the precedents in C−H alkynylation using these activated and polarized alkynes, the 2-iodobenzoic acid coproduct may further facilitate the activation of a C−H bond via a well studied carboxylate-assisted concerted metalation-deprotonation (CMD) mechanism.[18] As a continuation of our interest in C−H activation, we aimed to extend Rh(III)- and Ir(III)-catalyzed C−H functionalization to alkynylation using hypervalent iodine oxidants. We now report in full the efficient C−H alkynylation of a broad scope of arenes, including the substrate scope, selectivity, and mechanistic studies.

RESULTS AND DISCUSSION

Optimization of the Reaction Conditions. We initiated our studies with the screening of the conditions for the coupling of 2-(*m*-tolyl)pyridine with 1-[(triisopropylsilyl)-ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, Table 1). The 2-(*m*-tolyl)pyridine substrate was selected to ensure monoalkynylation selectivity. It was found that $[RhCp^*Cl_2]_2$ alone (4 mol %) exhibited no reactivity at room temperature. Increasing the reaction temperature to 80 °C only resulted in a low conversion (entry 2). While $Cu(OAc)_2$ proved to have no effect as an additive (entry 10), $Cu(OTf)_2$ improved the catalytic efficiency and afforded the expected alkynylation product (**3a**) in moderate yield (entry 5). Gratifyingly, addition of $AgSbF_6$, $Zn(OTf)_2$, or $Zn(NTf_2)_2$ gave comparably favorable results, and the yield of the product was dramatically improved even at room temperature (entries 2, 3, 6, 7). It is interesting to note that $AgSbF_6$ and zinc salts performed with comparable efficiency. Although the exact nature of active catalytic species is unclear, a cationic Rh(III) species is probably the real catalyst. $AgSbF_6$ is a well-known additive to activate the catalyst by chloride abstraction to give a cationic Rh(III) species. On the other hand, $Zn(OTf)_2$ may play a dual role in both activating the catalyst by reversible chloride abstraction and activating the alkyne substrate because $Zn(OTf)_2$ is known to electrophilically activate TIPS-EBX in gold catalyzed C−H alkynylation.[12c] Indeed, addition of $Zn(OTf)_2$ to $[RhCp^*(MeCN)_3](SbF_6)_2$ catalyst improved the catalytic efficiency (entries 11, 12). Therefore, for cost-effectiveness $Zn(OTf)_2$ was selected as the optimal additive. Control experiments revealed that no such coupling occurred in the absence of the rhodium catalyst, and switching the rhodium catalyst to the iridium congener resulted in essentially no conversion (entry 13). Gratifyingly, the catalyst loading can be reduced to 2 mol % without any loss of the activity, under which conditions product **3a** was isolated in 90% yield (entry 8).

Table 1. Optimization Studies[a]



entry	additive	temp (°C)	solvent	yield[b]
1	–	80	DCE	30%
2	$AgSbF_6$	25	DCE	89%
3	$AgSbF_6$[c]	25	DCE	86%
4	CF_3COOH	25	DCE	nd
5	$Cu(OTf)_2$	25	DCE	68%
6	$Zn(OTf)_2$	25	DCE	92%
7	$Zn(NTf_2)_2$	25	DCE	91%
8[d]	$Zn(OTf)_2$	25	DCE	90%
9	$Zn(NTf_2)_2$	25	DCM	85%
10	$Cu(OAc)_2$	25	DCE	nd
11[e]	-	25	DCE	20%
12[f]	$Zn(OTf)_2$	25	DCE	62%
13[g]	$AgSbF_6$	25	DCE	nd

[a]Reactions were carried out by using 2-(*m*-tolyl)pyridine (0.2 mmol), TIPS-EBX (0.22 mmol), $[RhCp^*Cl_2]_2$ (4 mol %), additive (20 mol % for salts and 1 equiv for CF_3COOH), solvent (2 mL), 25 °C, 16 h. [b]Isolated yield after column chromatography. [c]$AgSbF_6$ was used in 16 mol %. [d]$[RhCp^*Cl_2]_2$ (2 mol %) and $Zn(OTf)_2$ (10 mol %) were used. [e]$[RhCp^*(MeCN)_3](SbF_6)_2$ (4 mol %) was used as a catalyst. [f]$[RhCp^*(MeCN)_3](SbF_6)_2$ (4 mol %) was used as a catalyst in addition to $Zn(OTf)_2$ (20 mol %) [g]$[IrCp^*Cl_2]_2$ (4 mol %) was used in instead of $[RhCp^*Cl_2]_2$.

Substrate Scope. Following the optimized conditions, we next explored the scope and limitation of this system (Schemes 1 and 2). 2-Phenylpyridines bearing different electron-donating, -withdrawing, and halogen groups at the *ortho* and *meta* positions of the phenyl ring all coupled smoothly with TIPS-EBX with monoalkynylation selectivity. In contrast, a mixture of mono- and dialkynation products was obtained for substrates with the simple phenyl or *para*-substituted phenyl rings (**3p**−**3s′**). Fortunately, adjusting the stoichiometry of the substrates can further optimize the yield of both products. Thus the dialkynylation product can be obtained in high yield (**3t**−**3x**) when an excess of TIPS-EBX was used, and the mono-alkynylation products were isolated in moderate to good yield when an excess of the arene was used. The pre-installed formyl (**3p**, **3p′**), hydroxyl (**3r**, **3r′**), and halogen (**3b**, **3g**) groups in the product should readily allow further functionalization. Other alkynes such as TES-EBX, TBDPS-EBX, and ^{t}Bu-EBX also gave comparably high yield. In contrast, the reaction of TMS-EBX and 2-phenylpyridine gave moderate yield (**3l**), albeit with high monoselectivity. Here the decreased yield is likely due to the lower stability of the TMS-EBX or the product which lacks steric protection.[12c] The arene substrate is not limited to phenyl rings. C−H alkynylation of indoles bearing different electron-donating and -withdrawing groups reacted exclusively at the 2-position with different alkynes in consistently high efficiency (**3aa**−**3af**). The observed 2-alkynylation is dominated by the directing effect, which stands in contrast to the observed 3-alkynylation of protic indoles under gold catalysis,[12a,c] where the electrophilic C−H activation mechanism is operational. Although 2-alkynylation has been achieved by using palladium catalysis,[12b] the N-substituent is limited to an alkyl group. In addition to indoles, thiophenes also coupled in high efficiency (**3y**,**3z**). Besides the pyridine directing group, other heterocycles such as pyrimidine, pyrazole, and oxazoline are also competent, although a higher temperature is necessary for 2-phenylpyrimidines.

Substrate Scope. The scope of the directing group was further defined using a variety of readily functionalizable

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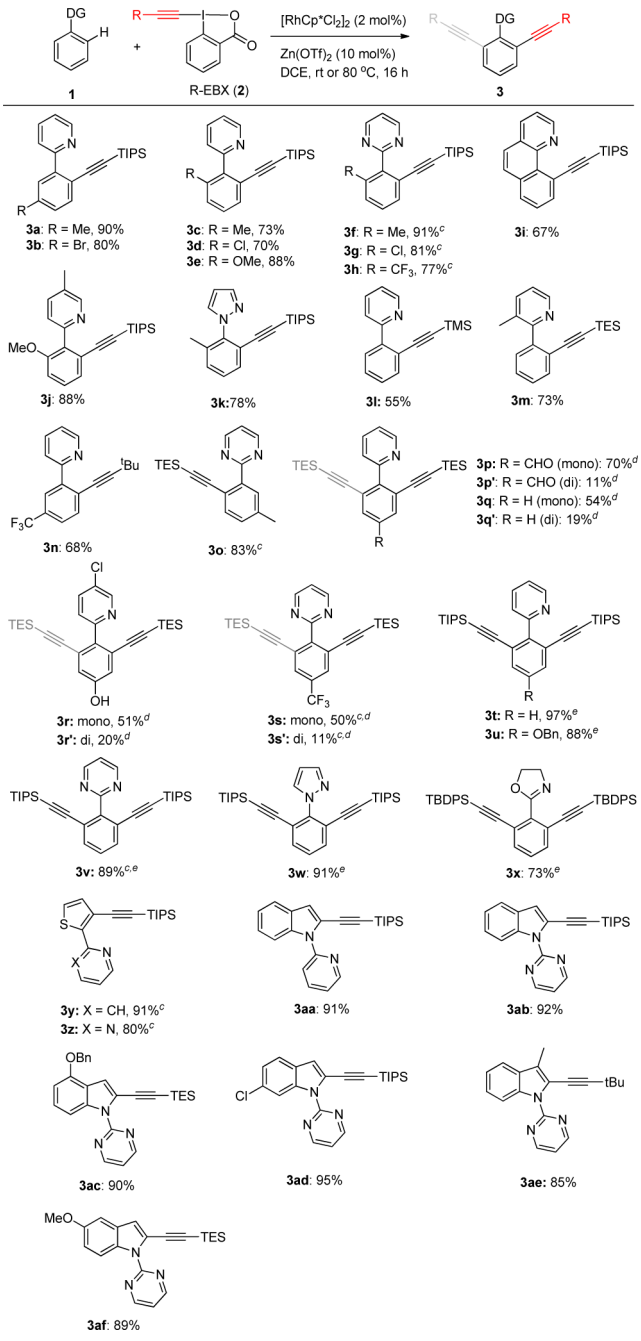
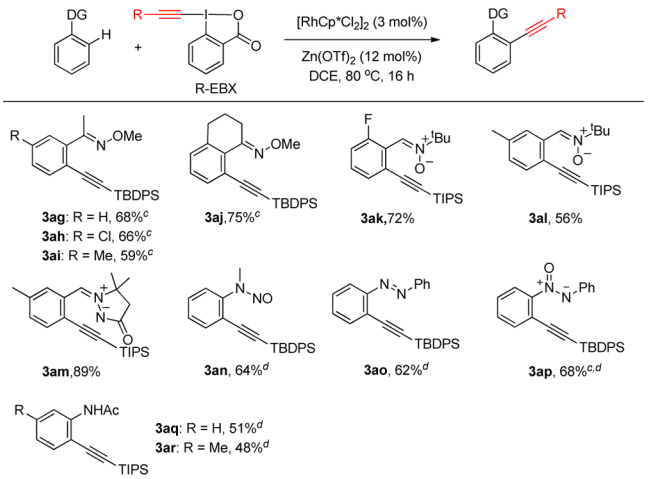
Scheme 1. C−H Alkynylation Assisted by Heterocyclic Directing Groups[a,b]



[a]Reactions conditions: arene (0.2 mmol), R-EBX (0.22 mmol), $[RhCp^*Cl_2]_2$ (2 mol %), $Zn(OTf)_2$ (0.02 mmol, 10 mol %), DCE (2 mL), 25 °C, 16 h. [b]Isolated yield after column chromatography. [c]Reaction was performed at 80 °C. [d]Arene (0.26 mmol) and the alkyne (0.2 mmol) were used. [e]Arene (0.2 mmol) and the alkyne (0.46 mmol) were used.

directing groups under modified conditions with 3 mol % of the rhodium catalyst (Scheme 2). A series of acetophenone *O*-methyl oximes reacted with TBDPS-EBX in the presence of $AgNTf_2$ additive (80 °C) to afford the monoalkynylation product in 59−75% yield (**3ag**−**3aj**), while lower yields were obtained when $Zn(OTf)_2$ were applied as an additive. Using nitrone oxygen as a directing group,[19] different *N*-*tert*-butyl-α-phenylnitrones coupled with TIPS-EBX to afford the

Scheme 2. C−H Alkynylation Assisted by Other Functionalizable Directing Groups[a,b]



[a]Reactions conditions: arene (0.2 mmol), alkyne (0.22 mmol), $[RhCp^*Cl_2]_2$ (3 mol %), $Zn(OTf)_2$ (0.024 mmol, 12 mol %), DCE (2 mL), 80 °C, 16 h. [b]Isolated yield after column chromatography. [c]$AgNTf_2$ (0.024 mmol) was used in lieu of $Zn(OTf)_2$. [d]Arene (0.26 mmol) and the alkyne (0.2 mmol) were used.

alkynylation products in good yields (**3ak**, **3al**) using $Zn(OTf)_2$ as an additive. These nitrone-alkyne analogues have been demonstrated by us and others to undergo Au(I)-, Ru(II)-, and Ir(III)-catalyzed cyclization via an internal redox pathway to afford useful heterocycles.[20] The C−H alkynylation reaction is readily applicable to a structurally related azomethine imine (**3am**) in high yield,[21] where the introduction of a *meta* methyl group ensured high monoselectivity. Otherwise, both mono and dialkynylation would occur. The arene substrate is not limited to derivatives of carbonyl groups. Thus *N*-nitrosoanilines[22] coupled with TBDPS-EBX to afford **3an** in 64% yield. Azobenzene (**3ao**) and azoxybenzene (**3ap**) also exhibited comparable reactivity and selectivity. Protic directing groups that form covalent bonds with rhodium are also applicable. Acetanilides coupled with monoselectivity, albeit in moderate isolated yield (**3aq**, **3ar**).

Alkynylation of *N*-Pivaloyloxybenzamides. This coupling reaction can be further extended to *N*-pivaloyloxybenzamide under modified, basic conditions. Thus product **4a** was isolated in high yield when CsOAc (20 mol %) was used as an additive in methanol (Scheme 3), and no dialkynylation product was detected. Under these operationally simple conditions, a series of *N*-pivaloyloxybenzamides bearing electron-donating and -withdrawing groups at different positions are tolerated, and the products were isolated in good to high yields (67−89%), although electron-poor *N*-pivaloyloxybenzamides tend to react with somewhat lower efficiency. The arene ring can also be extended to a thiophene (**4h**). However, attempts to achieve the C−H alkynylation of an olefinic substrate failed, and essentially no conversion was achieved (**4i**). The synthetically important C(O)NHOPiv group in these products should allow further diversified functionalization by Rh(III) catalysis.[23] In all cases, the rhodium catalyst is necessary as evidenced by control experiments.

Alkynylation of *N*-Methoxybenzamides by Iridium Catalysis. Since *N*-methoxybenzamides are analogues of *N*-pivaloyloxybenzamides and are known as important susbstrates

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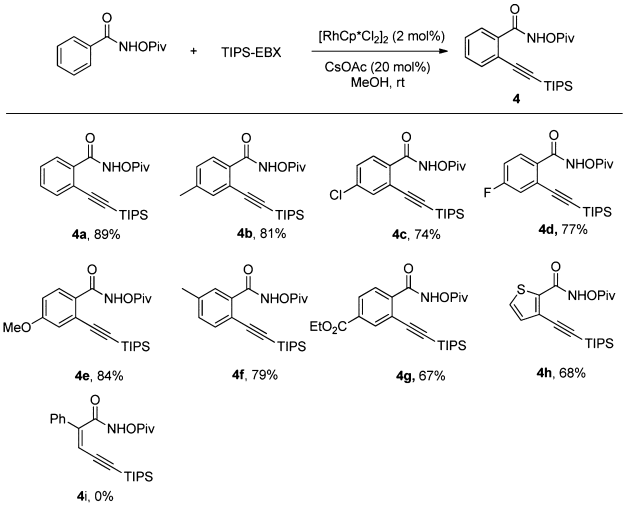
Scheme 3. Rh(III)-Catalyzed C−H Alkynylation of *N*-pivaloyloxybenzamides[a,b]

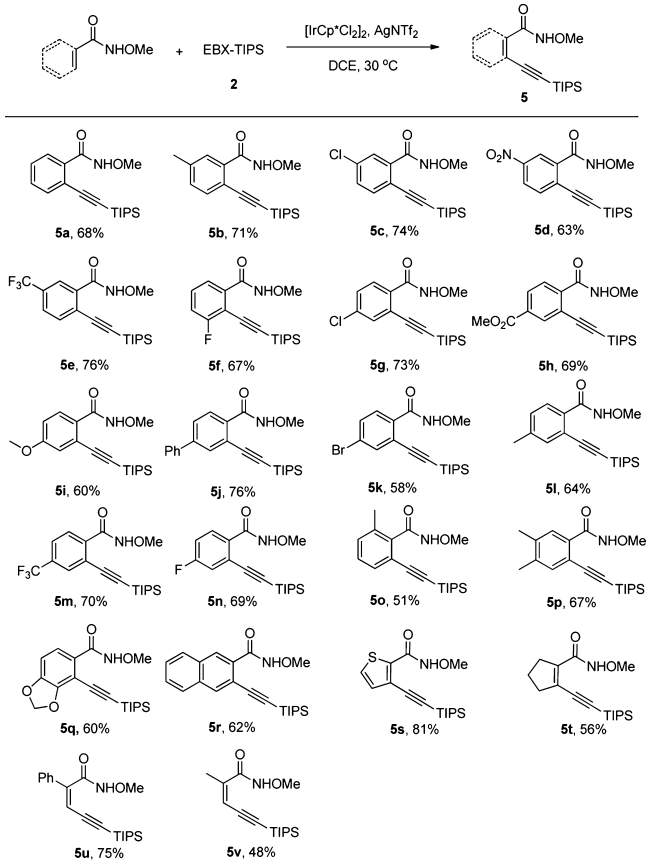


[a]Reactions conditions: *N*-pivaloyloxybenzamide (0.2 mmol), alkyne (0.22 mmol), $[RhCp^*Cl_2]_2$ (2 mol %), CsOAc (0.04 mmol, 20 mol %), MeOH (2 mL), 25 °C, 16 h. [b]Isolated yield after column chromatography.

in C−H activation,[24] were attempted the coupling of with TIPS-EBX under Rh(III)-catalyzed conditions. However, no desired coupling reaction occurred when the rhodium-catalyzed conditions in the Scheme 4 were followed. To our delight, although the $[IrCp^*Cl_2]_2$ complex failed to catalyze the alkynylation of 2-phenylpyridines, switching the rhodium catalyst to this iridium[25] congener (4 mol %) in the presence of $AgNTf_2$ (16 mol %) dramatically improved the reaction efficiency. Thus the coupling of *N*-methoxybenzamide with TIPS-EBX afforded **5a** as the major product (68%), and only a small amount (ca. 5%) of the dialkynylation product was isolated. Under the iridium-catalyzed conditions, a broad scope of such benzamides bearing a range of electron-donating and -withdrawing groups at different positions in the benzene ring are well-tolerated, and the yield of the isolated product ranges from 51% to 76%, with no obvious correlation between the yield and the electronic effect of the substituent. The isolated yield is even higher for a thiophene-2-carboxamide (**5s**). Furthermore, extension to olefinic substrates bearing this type of directing group proved successful (**5t**, **5u**, **5v**), where the products were isolated in essentially the same range of yield. This indicates that iridium and rhodium catalysts can offer complementary results in C−H activation of different substrates.

Synthetic Applications. Synthetic applications of some alkynylation products have been demonstrated (Scheme 5). While desilylation of **3a** using TBAF leads to decomposition due to product instability, protection by *N*-oxide formation followed by desilylation affords the terminal alkyne **7** (Scheme 5a). In contrast, alkyne **3ap** underwent smooth desilylation to afford **8**, and further metal-free cyclization to indole **9** has been documented (Scheme 5b).[26] Reductive denitrosylation of **3an** yielded aniline **10** in high yield. Desilylation to **10a** and subsequent cyclization with TsN_3 followed by acid hydrolysis is a known procedure to give indolinone **11** (Scheme 5c).[27] Treatment of **3ae** with NaOEt in DMSO led to removal of the pyrimidine directing group to afford a protic indole **12** (Scheme 5d). The alkynylated azobenzene **3ao** is known to cyclize to an

Scheme 4. Ir(III)-Catalyzed C−H Alkynylation of *N*-Methoxycarboxamides[a,b]



[a]Reactions conditions: arene (0.2 mmol), alkyne (0.22 mmol), $[IrCp^*Cl_2]_2$ (4 mol %), $AgNTf_2$ (0.032 mmol, 16 mol %), DCE (2 mL), 30 °C, 16 h. [b]Isolated yield after column chromatography.

isoindazole (**13**) by following a reported sequence (Scheme 5e).[28] In addition to these transformations, desilylation of **5a** by TBAF treatment triggered a cyclization to give two isomeric exocyclized olefins **14** (major) and **14′** (minor) (Scheme 5f).

Kinetic Isotope Effects. Some experiments have been performed to probe the reaction mechanism (Scheme 6). When rhodacyclic complex **15**[29] was applied as a catalyst (4 mol %) to the reaction of 2-(*m*-tolyl)pyridine and TIPS-EBX under otherwise the same conditions, product **3a** was isolated in nearly the same yield (Scheme 6a). This suggests that **15** is likely an active species or a direct precursor and C−H activation is involved. Thus KIE studies have been performed to gain further mechanistic details. The intermolecular competition between 2-PhPy and 2-PhPy-d_5 with TMS-EBX at ∼20% conversion gave KIE = 4.8 on the basis of ^{1}H NMR analysis. In this experiment TMS-EBX was used to remove complication of dialkynylation because essentially only the monoalkynylation product (**3l**) was generated, although the eventual isolated yield of this product was only moderate (55%, Scheme 1). Since TIPS-EBX coupled with higher efficiency than TMS-EBS, two different KIE measurements using TIPS-EBX were then performed. In one experiment, under the intermolecular competitive reaction conditions the coupling of 2-PhPy and 2-PhPy-d_5, essentially only the monoalkynylation product was detected at a low conversion (∼18% after 20 min), and k_H/k_D = 5.7 was obtained. In the other experiment, two independent and parallel coupling reactions of TIPS-EBX with

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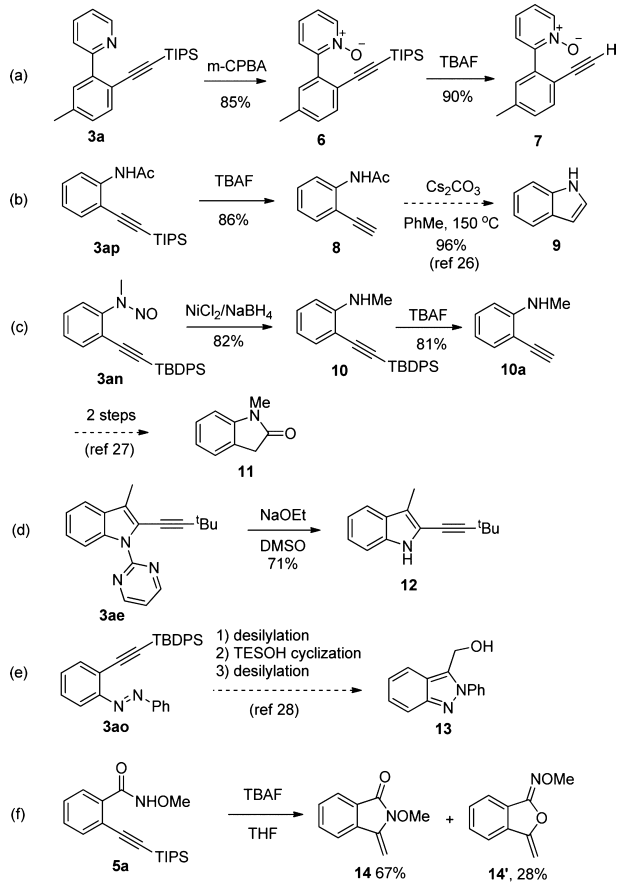
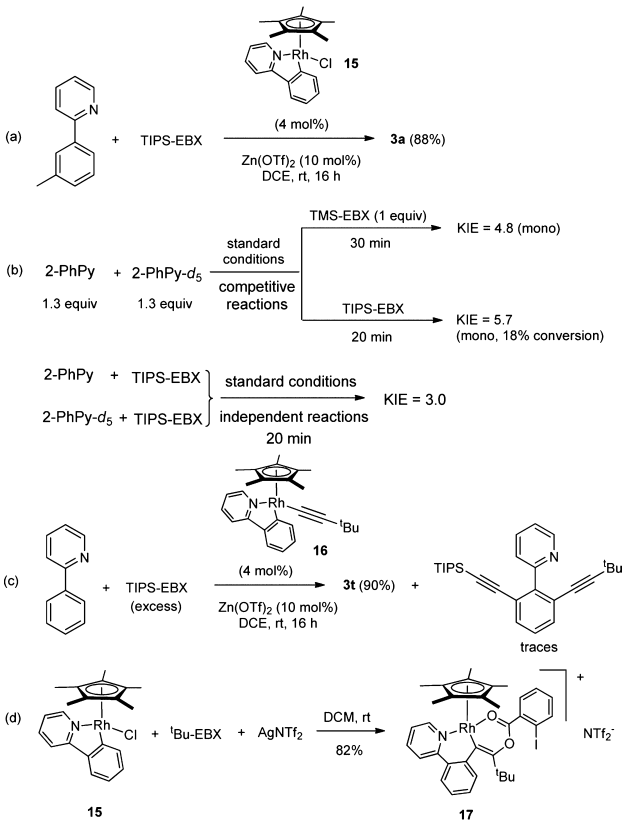
Scheme 5. Transformations of the Coupled Products



Scheme 6. Mechanistic Studies



2-PhPy and 2-PhPy-d_5 at a low conversion for both experiments gave k_H/k_D = 3.0 (Scheme 6b). All these values indicate that the cleavage of the *ortho* C−H bond is likely involved in the rate-limiting step. In line with the KIE values obtained by Rh(III) catalysis, a KIE = 2.3 was also obtained from the competitive coupling of PhC(O)NHOMe and PhC(O)NHOMe-d_5 by Ir(III) catalysis.

Rhodium Alkynyl Intermediate. We speculated that rhodium alkynyl species could be an intermediate in the catalytic cycle. Thus rhodium alkynyl complex **16** was prepared and was designated as a catalyst (4 mol %) for the coupling of 2-phenylpyridine with TIPS-EBX (Scheme 6c). Indeed, **16** exhibited comparable activity, and traces of the unsymmetrically dialkynylated product were also detected by GC-MS, indicating that **16** is probably an intermediate. To probe the relevancy of any organic radical species, TEMPO and BHT have been applied as radical inhibitors to the coupling of 2-(*m*-tolyl)pyridine and TIPS-EBX. The fact that the yield of the expected product **3a** was only marginally affected by either reagent (87% and 84%, respectively) suggests that a radical species seems less likely.

Isolation of Rhodium Vinyl Complex. To delve into the interaction of a cyclometalated Rh(III) aryl species with the hypervalent iodine-alkyne substrate, a stoichiometric reaction has been performed using an equimolar amount of complex **15**, ^{t}Bu-EBX, and $AgNTf_2$ (Scheme 6d). To our delight, although no Rh(V) species was obtained, an ester-functionalized Rh(III) alkenyl complex **17** (Scheme 6d) was isolated in high yield. Complex **17** was fully characterized by NMR spectroscopy and by X-ray crystallography. In particular, ^{1}H NMR spectroscopy revealed the incorporation of a unit of the ^{t}Bu-EBX, and in the ^{13}C NMR spectrum (CD_2Cl_2), the Rh−C(vinyl) signal resonates characteristically at δ = 139.2 (d, J_{Rh-C} = 27.8 Hz). The structure of **17** was unambiguously established by X-ray crystallography (Figure 1 and the SI), and it adopts a piano-stool structure bearing an N−C−O tripodal ligand. The ^{t}Bu group and the phenylene group stay *cis* to each other in the olefin unit.

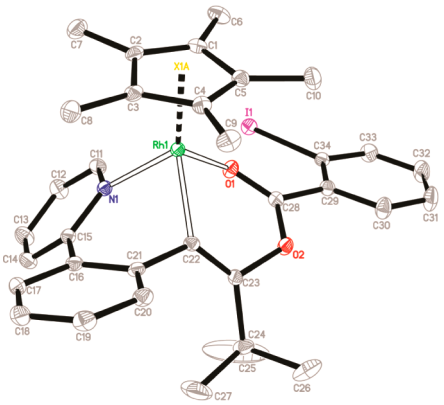


Figure 1. Molecular structure of complex **17** (cation only). Thermal ellipsoids are shown at a level of 30% probability.

Relevancy of the Rhdoium Vinyl Complex in Catalysis. Although no vinyl ester was observed as a product in the coupling of arenes with the R-EBX (*R* = silyl or ^{t}Bu) substrate, the relevancy of complex **17** in the catalytic system was evidenced using complex **17** as a catalyst (4 mol %) for the coupling of 2-PhPy and TIPS-EBX, from which the

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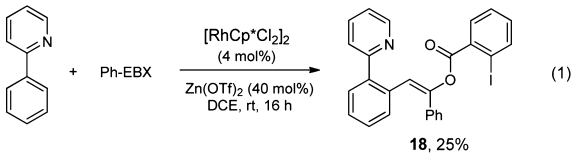
dialkynylation product **3t** was isolated in 85% yield together with the monoalkynylation product (7%). Further evidence on the role of complex **17** follows from the coupling of 2-PhPy and Ph-EBX, which is known to be a much less efficient alkynylating reagent likely due to lack of steric stabilization. Switching from the silyl-EBX to the Ph-EBX substrate gave rise to a less clean reaction. Nevertheless, a vinyl ester **18** was isolated as a major product in 25% yield, and the identity of this vinyl ester has been confirmed by NMR spectroscopy and by a simple derivatization reaction (eq 1 and SI). These results suggest that



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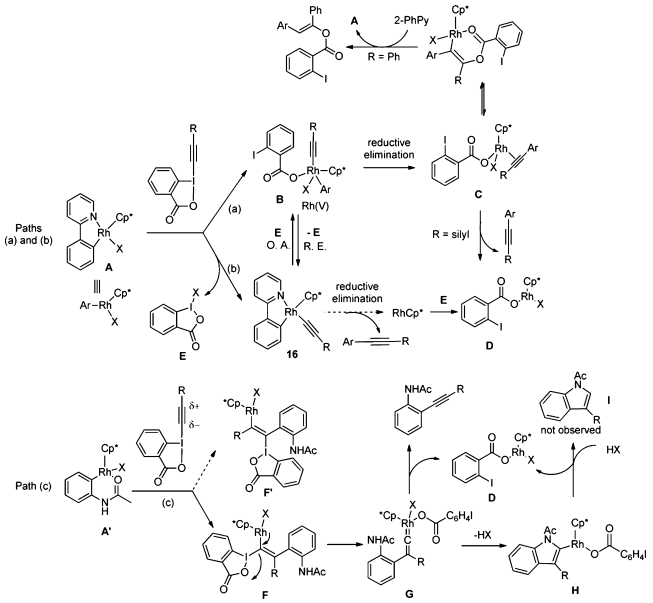
Rh(III) alkenyl complex **17** is likely an intermediate in the catalytic cycle and different types of products were obtained as a result of the stereo and electronic effects of the alkynyl group in the hypervalent iodine-alkyne reagent. To further probe the relevancy of complex **17** in the catalytic cycle, a stoichiometric reaction was performed using **17** and 2-PhPy (2.1 equiv) in DCM (50 °C, 16 h). Only a small amount of the monoalkynylation product was released from **17** and it was isolated in 10% yield. This indicates that the tripodal N−C−O ligand exhibits an inhibitive effect and that the elimination of the 2-iodobenzoate group is likely involved in the catalytic cycle (See Scheme 7).

Scheme 7. Mechanistic Proposals



Mechanistic Proposals. Given the observed experimental results, three possible mechanisms have been proposed (Scheme 7). In path (a), cyclometalation affords a rhodacyclic intermediate (**A**, where X = a weakly coordinating ligand), which oxidatively adds to the hypervalent iodine to give a Rh(V)[30] alkynyl (**B**). This oxidative addition could be facilitated by electrophilic activation of the alkyne reagent by the zinc or silver salt. Reductive coupling of **B** generates a Rh(III) alkyne benzoate intermediate **C.** This benzoate ligand is proposed to undergo reversible migratory insertion of the benzoate to afford an isolable rhodium(III) vinyl intermediate (**17**). In the case of the coupling for the Ph-EBX substrate, dechelation of complex **17** followed by coordination of 2-PhPy and subsequent cyclometalation releases the vinyl ester product (**18**).[31] Alternatively, for silyl-EBX substrates, alkyne dissociation from **C** released the final product together with a Rh(III) benzoate intermediate **D**. The catalyst is regenerated when carboxylate-assisted C−H activation occurs when a coordinated 2-phenylpyridine undergoes subsequent concerted metalation-deprotonation.[18] In pathway (b), transmetalation between **A** and the hypervalent iodine affords the alkynyl intermediate **16** and another hypervalent reagent **E**. Reductive elimination of **16** furnishes the final product and a Rh(I) species, which is oxidized by the hypervalent iodine reagent **E** to provide the same intermediate **D**. To probe this reductive elimination step, complex **16** was allowed to decay in CD_2Cl_2, but essentially no conversion occurred at 25 °C for 24 h in the presence or absence of 2-PhPy, which indicates that path (b) is less likely.

A third possible mechanism (Scheme 7, path c) with no metal alkynyl species is also proposed using acetanilide as a substrate. Rhodacyclic intermediate **A′** may undergo regioselective migratory insertion into the alkyne unit to give an alkenyl (**F**), and it should be noted that this regioselectivity is expected because the alternative insertion selectivity that generates **F′** is both sterically and electronically unfavorable. The α elimination of 2-iodobenzoate from **F** is then proposed to afford a Rh(III) vinylidene intermediate **G**. 1,2-Migration of the aryl (generally aryl tends to migrate preferentially to ^{t}Bu) in **G** followed by alkyne decoordination furnishes the coupled product. This pathway is less likely because in the case of an acetanilide, the Rh(III) vinylidene **G** is functionalized with a proximate nucleophilic group, which should intramolecularly trap the vinylidene[32] to eventually yield an indole product **I**. However, no such indole was detected by GC-MS, and the same scenario applies to PhC(O)NHOPiv (Scheme 3). Furthermore, the failure to observe any vinyl ether product in the synthesis of **4a** in methanol also argues against this mechanism because the MeOH solvent may intermolecularly trap the vinylidene. Therefore, on the basis of our rationale, we tend to favor the path (a) with a Rh(III)−Rh(V)−Rh(III) process.

■ CONCLUSION

We have developed the first Rh(III)- and Ir(III)-catalyzed efficient *ortho* C−H alkynylation of diversified arenes using hypervalent iodine-alkyne reagents.[33] The reaction conditions are mild, and both electron-poor and -rich arenes bearing a broad scope of DGs are viable substrates. Rhodium and iridium catalysts exhibited complementary substrate scope. In the case of N-heterocyclic directing groups, both mono- and dialkynylation may occur, and the selectivity is controllable. The synthetic utility of these alkynylation products has been demonstrated in synthetically useful derivatization reactions. A rhodium(III) alkynyl complex and a Rh(III) vinyl complex have been established as key intermediates. This system is complementary to previously known systems of C−H alkynylation of electron-rich (hetero)arenes under Au(I) and Pd(II) catalysis. The relatively mild conditions, broadly defined directing groups, tolerance of functional groups, and in some cases controllability of mono- and diselectivity may allow opportunity of synthetic applications.

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■ ASSOCIATED CONTENT

Supporting Information

Experimental details, spectroscopic data for all new compounds, and crystallographic data of complex **17** (PDF and CIF). 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.

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