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Rhodium–copper–TBAF-catalyzed hydroarylation of alkynes with aryl Trimethoxysilanes

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ABSTRACT

A rhodium–copper–TBAF-catalyzed hydroarylation of alkynes with aryl trimethoxysilanes is described. The procedure utilizes a catalytic amount of copper(II) acetate, rhodium, PPh_3 and $TBAF{\cdot}3H_2O$ under air. Some asymmetric alkynes gave the products with high regioselectivities.

The regio- and stereoselective synthesis of multi-substituted olefins has been a challenge for synthetic organic chemists for years.[1] Recently, much attention has been paid to rhodium-catalyzed hydroarylation of alkynes to access the aforementioned compounds.[2] Such hydroarylation and hydroalkenylation have already been attained by palladium- or nickel-catalyzed addition of organometallic compounds to the alkynes, or by titanium-catalyzed hydrozincation of alkynes.[3] Very recently, the transition-metal-catalyzed addition of arylboronic acids to unsaturated C–C bonds to achieve these analogues has drawn considerable attention due to the advantages of organoboron reagents.[4] However, either a coordinate or electron-withdrawing group was required in the reported addition of boronic acids to asymmetrical alkynes. Compared with the organoborons, organosilane reagents, especially aryl triethoxysilanes, are of lower cost[5] and easier to be purified by distillation or chromatography.[6] However, examples of employing organosilanes in this transformation were scarely reported or had limited substrates scope.[7] Herein, we wish to report rhodium–copper–TBAF-catalyzed hydroarylation of symmetrical and asymmetrical alkynes with aryl trimethoxysilanes, providing the tri-substituted alkenes in moderate to good yields (Fig. 1).

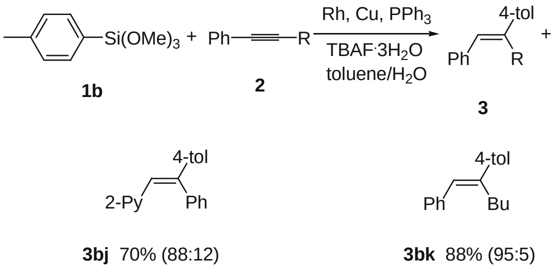
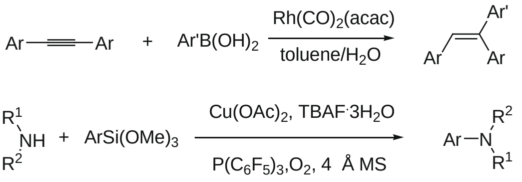


Figure 1. Hydroarylation of asymmetric alkynes. (Isolated yield with regioselective (**3**:**3**′ in parentheses), which were determined by ^{1}H NMR.)

Recently, we have developed a copper-catalyzed arylation of amines and amides employing aryl trimethoxysilanes, which were activated by catalytic amounts of TBAF.[8] We have also reported a phosphine-free rhodium-catalyzed hydroarylation of alkynes with boronic acids (Scheme 1).[9] Our interests in the development of transition-metal-catalyzed additions of arylmetallic reagents to the carbon–carbon or carbon–hetero unsaturated bonds[10] spur us to explore the possibility of using organosilanes activated by catalytic amounts of fluoride salts in such transformation.

Initial studies were conducted using the addition of phenyl trimethoxysilane **1a** to diphenyl acetylene **2a** as a model reaction. Unfortunately, the combination of PPh_3, $Cu(OAc)_2$ and a series of rhodium sources almost did not deliver the desired product (Table 1, entries 1–4). After intensive screening, we found that the product **3aa** was formed in 92% yield by employing Rh(cod)Cl dimer as rhodium source with the combination of PPh_3 and $Cu(OAc)_2$. Chloro bis(cyclooctene) rhodium(I) also gave the product in almost the same yield (Table 1, entry 5). Encouraged by this promising result, we tested other parameters, such as ligands and copper sources. Other copper salts were inferior to $Cu(OAc)_2$. The ligand also played an important role in the reaction. Among the phosphine ligands tested, monodent and bident and the ones bearing electron-rich or -deficient aryl groups all showed moderate activity in the reaction (Table 1, entries 12–18). However, the common and



Scheme 1. Our previous work.

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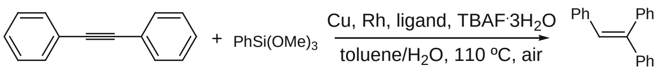
Table 1
Screening for the optimum conditions[a]



2a 1a 3aa

Entry	Rh source	Cu source	Ligand	Yield[b] (%)
1	Rh(cod)(acac)	$Cu(OAc)_2$	PPh_3	<5
2	$Rh(CO)_2(acac)$	$Cu(OAc)_2$	PPh_3	<5
3	$RhCl_3{\cdot}3H_2O$	$Cu(OAc)_2$	PPh_3	<5
4	$Rh(PPh_3)_3Cl$	$Cu(OAc)_2$	PPh_3	<5
5	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	PPh_3	92 (91)[c]
6	$[Rh(cod)Cl]_2$	$CuSO_4$	PPh_3	16
7	$[Rh(cod)Cl]_2$	$CuBr_2$	PPh_3	<5
8	$[Rh(cod)Cl]_2$	CuF_2	PPh_3	26
9	$[Rh(cod)Cl]_2$	$Cu(OTf)_2$	PPh_3	15
10	$[Rh(cod)Cl]_2$	$CuCl_2$	PPh_3	35
11	$[Rh(cod)Cl]_2$	CuI	PPh_3	52
12	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	$P(2\text{-}MeC_6H_4)_3$	<5
13	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	$P(3,5\text{-di-}MeC_6H_3)_3$	23
14	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	$P(4\text{-}MeOC_6H_4)_3$	25
15	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	dppe	28
16	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	$P(C_6F_5)_3$	37
17	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	P(1-naph)$_3$	57
18	$[Rh(cod)Cl]_2$	$Cu(OAc)_2$	$P(4\text{-}ClC_6H_4)_3$	<5
19	$[Rh(cod)Cl]_2$		PPh_3	<5

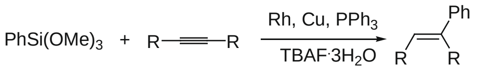
[a] All reactions were run with phenyl trimethoxysilane (59.4 mg, 0.3 mmol), diphenyl acetylene (36 mg, 0.2 mmol), Cu source (10 mol %), $TBAF{\cdot}3H_2O$ (6.3 mg, 10 mol %), ligand (10 mol %), Rh source (10 mol %) and solvent (3.05 mL, toluene/H_2O = 60:1) under air at 110 °C for 24 h.
[b] Isolated yield.
[c] Chlorobis(cyclooctene) rhodium(I) as rhodium source.

commercial available PPh_3 was the best. The presence of a proper portion of H_2O is crucial to the reaction. The reaction did not proceed in dry toluene, and excess H_2O decreased the yield. Higher yield was obtained when the reaction was carried out under air instead of under nitrogen. Thus, the rigorous exclusion of air/moisture is not required in this transformation.

With the optimized reaction conditions in hand, we then explored the scope of alkynes, as shown in Table 2.

As expected, all the reactions proceeded smoothly and provided the desired products in moderate to good yields. The hindrance of the alkynes had some effect on the reaction, for example, 66% and 73% of **3ab** and **3ah** were isolated, respectively (Table 2, entries 2 and 8). It is noteworthy that **3ah** is difficult to be prepared from corresponding organoboron in Hayashi's procedure since a 1,4-rhodium shift occurs in the catalytic cycle.[4c] However, in our procedure, **1a** reacted smoothly with **2h**, and produced the product **3ah** in 73% isolated yield (Table 2, entry 8). The presence of electron-donating substituents on the phenyl ring decreased the yields. Notably, the dialkyl acetylene, 3-hexyne **2j** was also a good reaction partner under the conditions (Table 2, entry 10), albeit **3aj** was isolated in moderate yield.

Table 2
Hydroarylation of alkynes with $PhSi(OMe)_3$[a]



1a 2 3

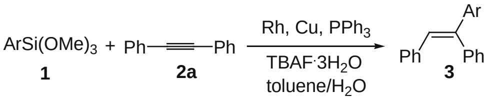
Entry	R	Product	Yield[b] (%)
1	Ph **2a**	**3aa**	90
2	$2\text{-}MeC_6H_4$– **2b**	**3ab**	66
3	$3\text{-}MeC_6H_4$– **2c**	**3ac**	71
4	$4\text{-}MeC_6H_4$– **2d**	**3ad**	80
5	$4\text{-}MeOC_6H_4$– **2e**	**3ae**	57
6	1-Naphthalenyl **2f**	**3af**	76
7	2-Naphthalenyl **2 g**	**3ag**	87
8	2,6-Di-Me-C_6H_3– **2 h**	**3ah**	73
9	3,5-Di-Me-C_6H_3– **2i**	**3ai**	90

[a] Reaction conditions: $PhSi(OMe)_3$ (59 mg, 0.3 mmol), diaryl acetylene (0.2 mmol), $Cu(OAc)_2$ (3.6 mg, 10 mol %), $TBAF{\cdot}3H_2O$ (6.3 mg, 10 mol %), PPh_3 (5.2 mg, 10 mol %), $[Rh(cod)Cl]_2$ (4.9 mg, 5 mol %) and toluene/H_2O (3.05 mL, 60:1) under air at 110 °C for 12 h.
[b] Isolated yield.

Next, we turned our attention to broaden the scope of aryl trimethoxysilanes. A series of $ArSi(OMe)_3$ were tested in the reaction condition and all delivered the product in moderate to good yields. The hindrance on the aryl group of $ArSi(OMe)_3$ had little effect on the reaction. For example, **3ca** and **3fa** were isolated in 91% and 73% yields, respectively (Table 3, entries 2 and 5). However, the feasibility of access to highly hindered triaryl ethene by using 2,6-di-$MeC_6H_3Si(OMe)_3$ and diphenyl acetylene failed (Table 3, entry 4).

Having demonstrated the utility of an addition reaction condition on a number of symmetrical diaryl alkynes, we chose to test the generality of the addition to asymmetrical internal alkynes. Employing 2-(2-phenylethynyl)pyridine **2m** as the substrate, the product **3bj** was delivered in 70% yield with 88:12 regioselectivity. The pyridin-2-yl attached in the triplet C–C bonds may coordinate with rhodium to increase the regioselectivity.[11] It is noteworthy that high regioselectivity was obtained when aryl alkyl acetylene was used as substrate. For example, **3bk** was isolated in 88% yield with 95:5 regioselectivity. To the best our knowledge, the asymmetrical addition of arylboronic acids to aryl alkyl acetylene were rarely studied before.[4c] As such, this represents an exceedingly practical method for the synthesis of tri-aryl-substituted olefins, and offers an attractive alternative to traditional organoboron addition procedures.

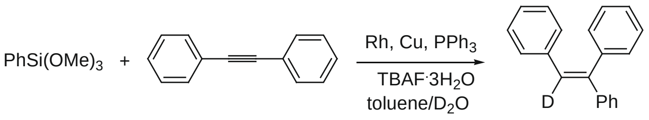
Table 3
Hydroarylation of diphenyl acetylene with $ArSi(OMe)_3$[a]



1 2a 3

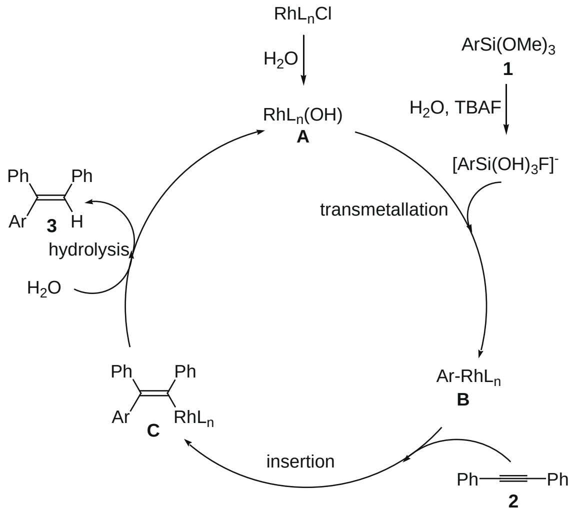
Entry	Ar	Product	Yield[a,b] (%)
1	$4\text{-}MeC_6H_4$– **1b**	**3ba**	80
2	$2\text{-}MeC_6H_4$– **1c**	**3ca**	91
3	$3\text{-}MeC_6H_4$– **1d**	**3da**	63
4	2,6-Di-MeC_6H_3– **1e**	**3ea**	<5
5	$2\text{-}MeOC_6H_4$– **1f**	**3fa**	73
6	$4\text{-}MeOC_6H_4$– **1g**	**3ga**	63
7	1-Naphthalenyl **1h**	**3 ha**	50
8	2-Naphthalenyl **1i**	**3ia**	57
9	3,5-Di-MeC_6H_3- **1j**	**3ja**	82

[a] Reaction conditions: $ArSi(OMe)_3$ (0.3 mmol), diphenyl acetylene (36 mg, 0.2 mmol), $Cu(OAc)_2$ (3.6 mg, 10 mol %), $TBAF{\cdot}3H_2O$ (6.3 mg, 10 mol %), PPh_3 (5.2 mg, 10 mol %), $[Rh(cod)Cl]_2$ (4.9 mg, 5 mol %) and toluene/H_2O (3.05 mL, 60:1) under air at 110 °C for 12 h.
[b] Isolated yield.



1a 2a **3aa'**, yield: 62%

Scheme 2. Labeling study.



Scheme 3. Plausible mechanism.

Labelling studies were conducted, and the result clearly showed that the H attached to the C=C bond derived from the solvent (Scheme 2). Moreover, the fact that product **3ah** was formed in 73% also ruled out the possibility of 1,4-rhodium shift.[4c]

A plausible mechanism is outlined in Scheme 3. The water may play three roles in this transformation: (1) promote the hydrolysis of the aryl trialkoxysilane to the corresponding aryl silanol, which is considered to be the actual reagent;[12] (2) hydrolyze the rhodium precatalyst into RhL$_n$ *(OH) and (3) hydrolyze* the rhodium species formed via the insertion of aryl rhodium species into the triplet bond, and regenerate the rhodium catalyst. However, the detailed mechanism, especially the catalytic cycle of the fluoride and the role of Cu(OAc)$_2$, is still unclear.

In conclusion, we have developed an efficient and versatile rhodium-catalyzed addition of ArSi(OMe)$_3$ to alkynes, providing the hydroarylation products in moderate to good yields. The wide range of substrates, the high regioselectivities for some asymmetric alkynes, as well as the utilization of the catalytic amount of TBAF as additive all together are the most attracting characteristics of this reaction. Furthermore, the rigorous exclusion of air/moisture is not required in these transformations. Mechanistic investigations and the application of the ArSi(OMe)$_3$ activated by catalytic amount of TBAF to other unsaturated bonds are now in progress.[13]

Acknowledgments

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13. *General procedure*: A reaction tube was charged with ArSi(OMe)$_3$ (0.3 mmol), Cu(OAc)$_2$ (3.6 mg, 10 mol %), TBAF·3H$_2$O (6.3 mg, 10 mol %), PPh$_3$ (5.2 mg, 10 mol %), [Rh(cod)Cl]$_2$ (4.9 mg, 5 mol %), toluene (3 mL) and alkynes (0.2 mmol) under atmosphere at room temperature. After stirring for 2 h, 60 μL of water was added, and the reaction mixture was continued to be stirred under atmosphere at reflux for 12 h. After the completion of the reaction, as monitored by TLC, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on a silica gel to give the product.