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Rh(I)-Catalyzed Cross-Coupling of α-Diazoesters with Arylsiloxanes

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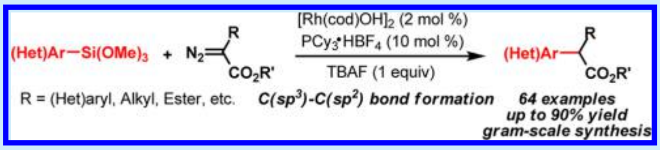
Supporting Information



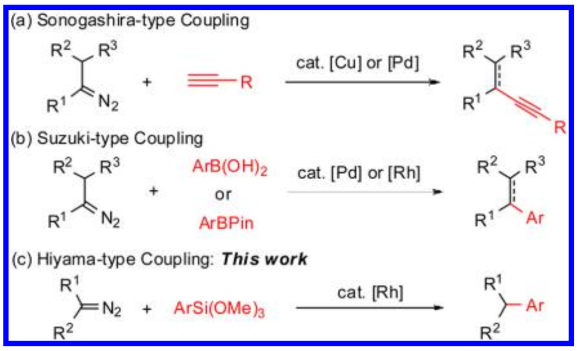
ABSTRACT: An Rh(I)-catalyzed cross-coupling of diazoesters with arylsiloxanes has been successfully achieved. This transformation is a new method for the construction of the C(sp^3)−C(sp^2) bond, thus providing an alternative synthesis of α-aryl esters. Rh(I)−carbene migratory insertion has been proposed to be involved in this coupling reaction. The reaction represents the first example of utilizing arylsiloxane as the coupling partner in the carbene-involved cross-coupling reactions.

Transition-metal-catalyzed cross-coupling reactions have been established as indispensible tools for carbon−carbon bond formation in modern organic synthesis. In this area, organosilicon reagents (Hiyama reaction and Hiyama−Denmark reaction) represent attractive coupling partners due to their facile availability, low toxicity, relative stability, and good functional-group compatibility when compared to other organometallic reagents.[1,2] Apart from the classical and/or modified coupling reactions with aryl halides[3] as the electrophiles, organosilicon reagents can also couple with alkynyl halides[4] and alkyl halides,[5] including the more challenging unactivated alkyl halides.[5a−c] In addition, organosilicon reagents also have been applied to C−H[6] and C−C[7] bond couplings under suitable catalytic reaction systems.

On the other hand, diazo compounds, including those generated in situ from the corresponding *N*-tosylhydrazones under basic conditions, have recently emerged as a new type of cross-coupling partners in transition-metal-catalyzed reactions.[8] The cross-coupling of diazo compounds with organometallic and related reagents represents a unique method for the construction of C−C bonds.[9,10] For example, in 2004, Fu and co-workers reported a Cu(I)-catalyzed Sonogashira-type coupling of diazo compounds with terminal alkynes in which the 3-alkynoate products are difficult to synthesize using the traditional Sonogashira reaction.[9a] This type of coupling reaction was further developed by the groups of Wang[9b] and Ma,[9c] who employed different types of diazo precursors to obtain the Sonogashira-type products by forming C(sp^3)−C(sp) bonds. Moreover, the Pd(II)-catalyzed Sonogashira-type coupling of diazo compounds or *N*-tosylhydrazones was reported to afford conjugated enynes (Scheme 1, a).[9d] The Suzuki-type coupling of diazo compounds was first realized with the catalysis of Pd complexes under oxidative conditions.[10a] Subsequently, this coupling reaction was expanded by employing Rh(I) catalysts (Scheme 1, b).[10d,11]

As a continuation of our interest in cross-coupling reactions of diazo compound, we turned our attention to a Hiyama-type coupling of organosilicon reagents with diazo compounds. However, compared to the corresponding Suzuki-type coupling, some challenges exist for the development of this type of coupling reaction: (1) the low polarizability of the C−Si bond in organosilicons requires special bases for transmetalation, which may decompose the labile diazo substrates; (2) the oxidant required for the regeneration of the Pd catalysts may not be compatible with the diazo compounds that are labile to oxidation. To our knowledge, the coupling reactions between organosilicons and diazo compounds for C−C bond formation are not known in the literature. Herein, we report the first Hiyama-type coupling of diazo compounds under the catalysis of Rh(I) complex (Scheme 1, c).

Scheme 1. Cross-Coupling Reactions with Diazo Compounds



Initially, the reaction of phenylsiloxane **1** and diazoester **2a** were carried out with Pd(PPh_3)$_4$ as the catalyst under oxidative conditions. However, the expected coupling product **3** was either not observed or only formed in very low yield with benzoquinone (BQ) or $CuCl_2$ as the oxidant (Scheme 2, a). Further optimization under palladium catalysis failed to improve the yield, which indicates that the diazoester, the oxidant, and TBAF are incompatible in one reaction system. We then turned our attention to rhodium catalysis, in which the oxidant is not needed because the terminating step of the catalytic cycle is the protonation instead of β-H elimination. Gratifyingly, the

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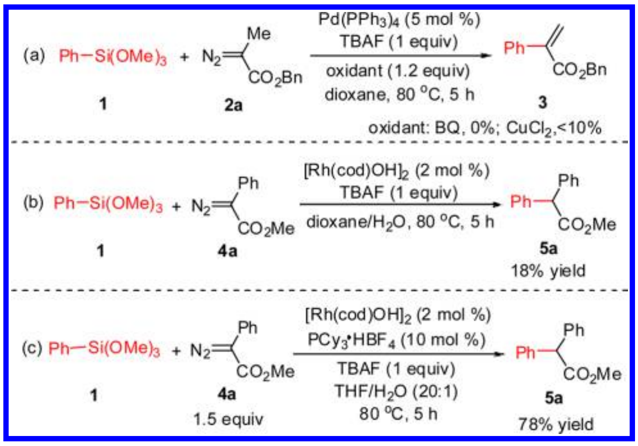
Scheme 2. Cross-Coupling of Phenylsiloxane with Diazoester: (a) Initial Attempt with Pd Catalysis; (b) Initial Attempt with Rh Catalysis; (c) Optimized Reaction Conditions with Rh Catalysis



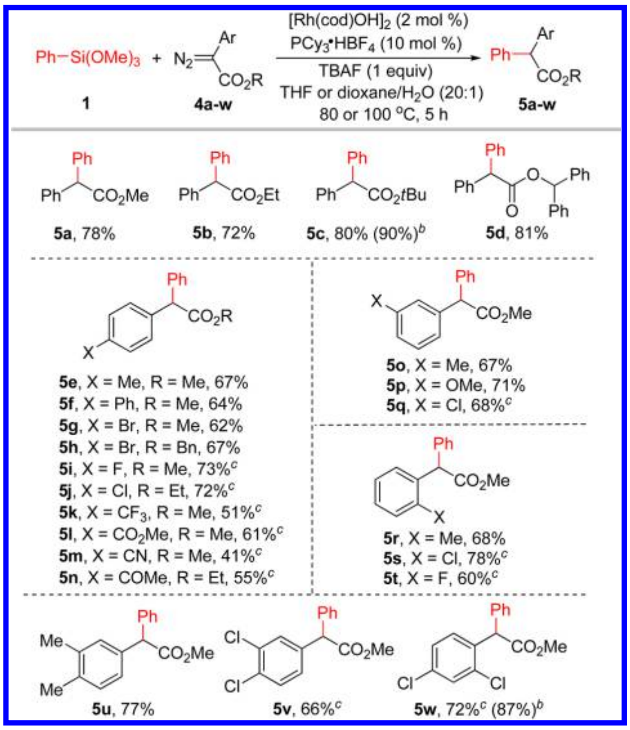
coupling of phenylsiloxane **1** with donor−acceptor diazoester **4a** under rhodium catalysis could afford the expected product **5a** in 18% isolated yield (Scheme 2, b).

With this initial result, further optimization of the reaction conditions was carried out. Through screening the reaction parameters, we concluded that the product **5a** could be isolated in 78% yield under the optimized conditions as shown in Scheme 2, c.[12] Since α-aryl esters are a class of important molecules in various fields,[13] we then proceeded to explore the scope of this Rh(I)-catalyzed Hiyama-type coupling. A series of aryl diazoesters (**4a−w**) were initially tested with phenylsiloxane **1** under the optimized reaction conditions (Scheme 3). The ester group on the diazo compound showed a negligible effect on this transformation, and the corresponding products were obtained in 72−81% yields (**5a−d**). The reactions with *para*- (**4e−n**), *meta*- (**4o−q**), and *ortho*-substituted (**4r−t**) aryl diazoesters as well as the multisubstituted diazo compounds (**4u−w**) all proceeded well, giving the corresponding coupling products in good yields.

For the more stable diazo compounds that bear electron-withdrawing substituents (**4i−n,q,s,t,v,w**), it was noted that higher reaction temperature was necessary. The reactions with these diazoesters were carried out at 100 °C in dioxane. Under such conditions, the diazo compounds could be fully converted with satisfactory yields. Notably, the chloro and bromo substituents are tolerated in this reaction, providing the opportunity for further transformations through transition-metal-catalyzed coupling reactions. In addition, the enolizable ketone moiety is also tolerated (**5n**), while such a moiety is not compatible with the Pd-catalyzed α-arylation of esters due to the strong basic conditions.

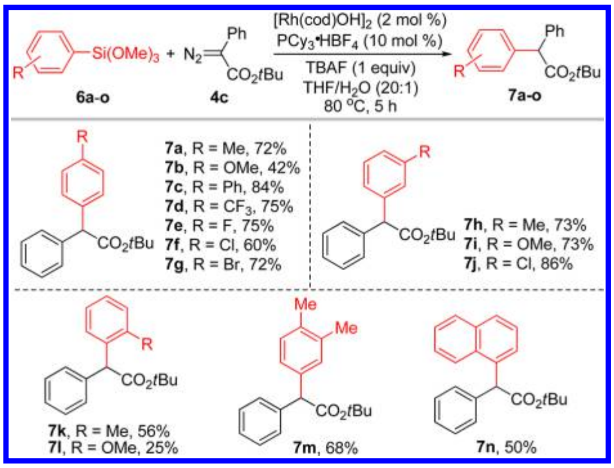
The operability and the efficiency of this Rh(I)-catalyzed carbene coupling was demonstrated by scale-up experiments. Under the same reaction conditions, the electron-neutral and electron-deficient aryl diazoesters were both scaled up to gram synthesis, and the corresponding diaryl acetates **5c** and **5w** could be obtained in 90% (1.21 g) and 87% (1.28 g) yields, respectively.[12] Notably, the yields of the gram-scale synthesis were 10−15% higher than that of the small-scale reactions.

Scheme 3. Reaction Scope of Aryl Diazoesters[a]



[a]Reaction conditions: $[Rh(cod)OH]_2$ (2 mol %), $PCy_3{\cdot}HBF_4$ (10 mol %), TBAF (0.2 mmol), **4a−w** (0.2 mmol), **1** (0.3 mmol), H_2O (200 μL), THF (4.0 mL), 80 °C under N_2 for 5 h, isolated yields. [b]Yield in parentheses was for the reaction on a 5 mmol scale. [c]The reaction was carried out in dioxane at 100 °C with 2 equiv of **1**.

Scheme 4. Reaction Scope of Arylsiloxanes[a]

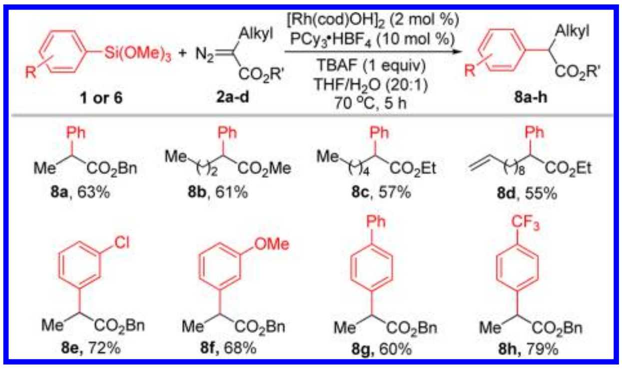


[a]The reaction conditions are the same as described in Scheme 3.

Next, the scope of arylsiloxanes **6a−o** was investigated by reacting with aryl diazoester **4c** under the optimized reaction conditions (Scheme 4). The coupling reaction with *para*- (**6a−g**) and *meta*-substituted (**6h−j**) arylsiloxanes worked well in this transformation, while the reaction with *ortho*-substituted arylsiloxanes (**6k−l**) only gave diminished yields. This is presumably attributed to the steric hindrance of the *ortho* substituents. In addition, the electron-rich substituents on the *para*- or *ortho*-position of the aryl ring were found to have negative effects on this transformation, as shown by the diminished yields in the cases of **7b** and **7l**. On the contrary, arylsiloxanes bearing electron-withdrawing substituents generally afforded the corresponding products in good to excellent yields (**7c−g,j**). Again, arylsiloxanes containing chloro or bromo groups worked well in this reaction (**7f−g,j**). Finally, naphthylsiloxane proved to be a suitable coupling partner, affording the corresponding product **7n** in 50% yield.

Apart from aryl diazoesters, the alkyl-substituted diazoesters were also explored. The alkyl diazoesters were found to be suitable substrates for this transformation at lower reaction temperature, giving products **8a–h** in moderate to good yields (Scheme 5). A series of alkyl diazoesters **2a–d** were reacted smoothly with phenylsiloxane (**8a–d**). It is noted that the terminal C–C double bond remains intact in this transformation, indicating that the high chemo-selectivity for the reaction between arylsiloxane and diazo moiety in the Rh(I)-catalyzed reaction (**8d**). Substituted arylsiloxanes also show good reactivity to alkyl diazoester **2a**, providing the corresponding aryl propanoates **8e–h** in good yields.

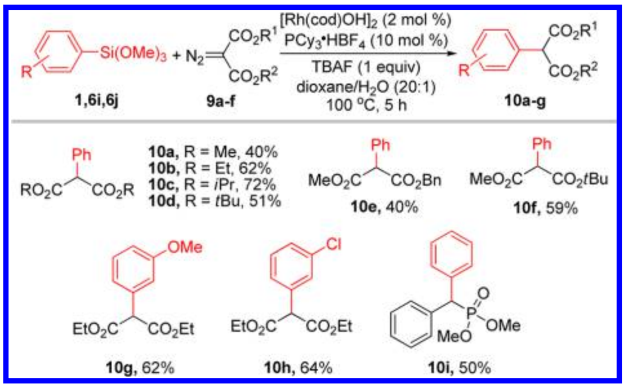
Scheme 5. Reaction Scope of Alkyl Diazoesters[a]



[a] The reaction conditions are the same as described in Scheme 3, except 2 equiv (0.4 mmol) of arylsiloxane was used and the reaction was carried out at 70 °C.

Then more stable diazo compounds, which bear two electron-withdrawing groups, were investigated. It was noted that such diazo compounds require elevated temperature for the reaction to complete, similar to that of the electron-deficient aryl diazoesters (Scheme 6). Under such conditions, a series of symmetric (**9a–d**) and unsymmetric (**9e–f**) diazomalonates were smoothly converted to the corresponding α-aryl malonates in 40–72% yields. Both electron-deficient and electron-rich arylsiloxanes participate in this transformation (**10g,h**). In addition, the α-aryl diazophosphonate was also a suitable substrate in this Rh(I)-catalyzed reaction, providing diaryl phosphonate **10i** in moderate yield.

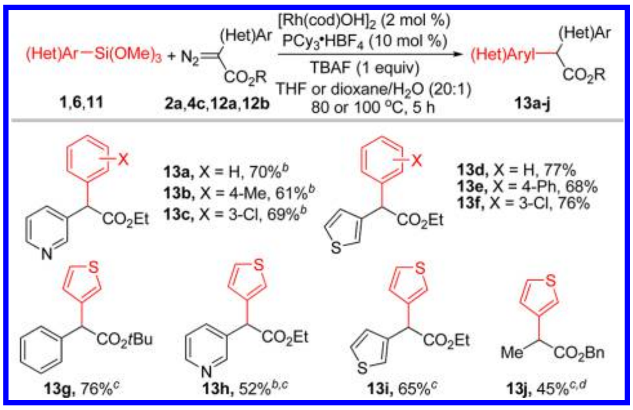
Scheme 6. Reaction Scope of Diazomalonates[a]



[a] The reaction conditions are the same as described in Scheme 3, except 2 equiv (0.4 mmol) of arylsiloxane was used and the reaction was carried out at 100 °C in dioxane.

Finally, the Rh(I)-catalyzed Hiyama-type coupling was applied to the synthesis of α-heteroaryl esters, which are difficult to access through other methods. As illustrated in Scheme 7, a range of α-heteroaryl esters could be obtained with the present method. Heteroaryl diazo compounds, such as 3-pyridinyl (**12a**) and 3-thienyl (**12b**) diazoesters, could smoothly undergo the coupling reaction with a series of arylsiloxanes. Furthermore, heteroarylsiloxane could also react with different types of diazo compounds to afford the corresponding products **13g–j**. Notably, the unsymmetric (**13h**) and symmetric (**13i**) diheteroaryl acetates could be readily accessed via this method.

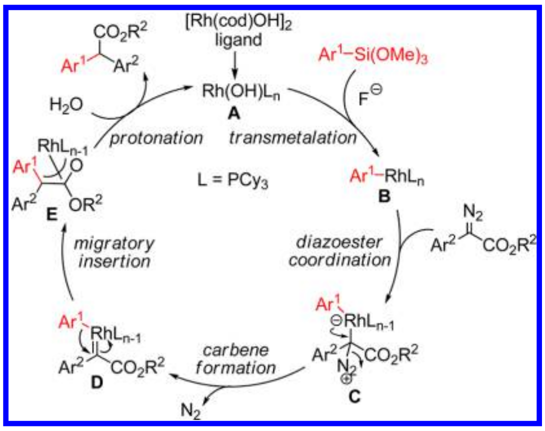
Scheme 7. Synthesis of α-Heteroaryl Esters[a]



[a] Unless otherwise noted, the reaction conditions are the same as described in Scheme 3. [b] The reaction was carried out in dioxane at 100 °C with 2 equiv (0.4 mmol) of arylsiloxane. [c] The reaction was carried out with 2.5 equiv (0.5 mmol) of 3-thienylsiloxane. [d] The reaction was carried out at 70 °C.

A tentative mechanism was proposed in Scheme 8.[12] Initially, [Rh(cod)(OH)]$_2$ dedimerizes and then undergoes ligand exchange with PCy$_3$ to generate an active catalyst species **A**, which undergoes transmetalation with arylsiloxane to form aryl Rh(I) intermediate **B** with the aid of TBAF.[14] Subsequently, the coordination of the aryl diazoacetate to rhodium center generates an η^1-C diazo complex **C**. For this step, the electron-donating substituents on the aryl diazoacetate substrates should facilitate the coordination. Dinitrogen extrusion then occurs from intermediate **C** to generate a Rh(I)–carbene complex **D**,[15]

Scheme 8. Proposed Reaction Mechanism



which then undergoes migratory insertion to afford oxa-π-allyl Rh(I) intermediate **E**.[16] Finally, **E** is protonated with H_2O to deliver the coupling product with the regeneration of the catalyst **A**.

In conclusion, we have reported the first Rh(I)-catalyzed Hiyama-type cross-coupling reaction between arylsiloxanes and diazoesters. A series of diazo compounds, including aryl, alkyl, and heteroaryl diazoesters as well as diazomalonates, participate in this reaction.[17] This transformation shows good functional group compatibility and can be scaled up, thus constituting an alternative method to the previously established Ni- and Pd-catalyzed synthesis. Finally, this reaction is an excellent example to demonstrate the fact that the merging of carbene chemistry with cross-coupling is generally applicable to various coupling partners.[8c]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, spectral data, and ^1H and ^{13}C NMR spectra for products. These materials are 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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(17) We have also attempted the cross-coupling with *N*-tosylhydrazone and aryldimethylsilanol as the substrates, but the reactions failed to afford the expected coupling products. For details, see the Supporting Information.

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