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Ethylaluminum as Ethylene Source for the Mizoroki-Heck-type Reaction. Rhodium-catalyzed Preparation of Stilbene Derivatives

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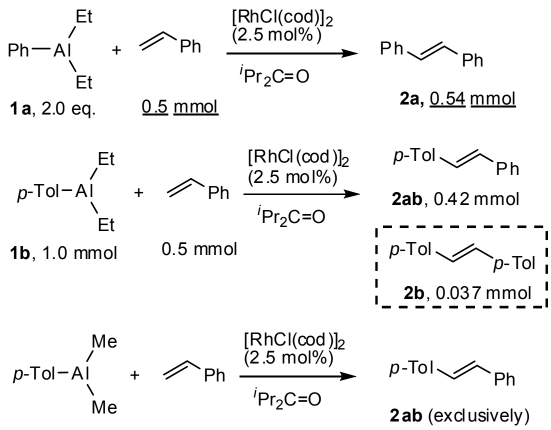
Treatment of organoaluminum reagent bearing aryl and ethyl groups furnishes 1,2-diarylethene derivatives in good to excellent yields by the catalysis of a rhodium complex, in which the ethyl group of aluminum reagent serves as ethylene source in the product.

Incorporation of small molecules such as carbon monoxide, carbon dioxide, hydrogen, nitrogen, oxygen, etc. into organic compound is an attractive issue for the functionalization of the organic framework in organic synthesis. Transition metal as a catalyst plays a key role for the reaction with small molecules, where gaseous reagents have been utilized in a certain reaction.[1] Several surrogate organic compounds as synthetic equivalents have been employed for reagents to avoid the use of occasionally toxic or explosive gasses, e.g. aldehyde as CO source etc.[2] Several metallic alkyls have also been employed as synthetic equivalent of the metal hydride for the reduction of carbonyl compounds through β-hydride elimination accompanied by the formation of corresponding olefin.[3] Compared with the use of metal alkyls as a reducing agent as hydride, little attention of the produced olefin toward a building block of organic compounds has been paid so far.[4]

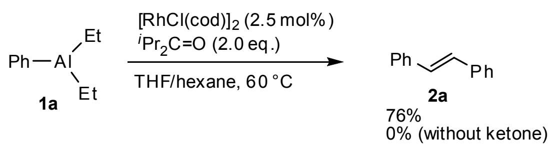
On the other hand, reactions with rhodium catalyst have been widely used as essential tools in forming a variety of C-C bond in organic synthesis.[5] In particular, various reactions using organometallic species (boron, silane, zinc, tin, aluminum, etc.) as a nucleophile such as cross coupling with organic halide,[6] conjugated addition to enones,[7] 1.2-addition to carbonyl compounds,[8] and oxidative Mizoroki-Heck type reaction toward olefins[9] have been developed so far. We have shown related Mizoroki-Heck type reactions of organosilicon species with olefin in the presence of a rhodium or iridium catalyst[10] and we have recently reported that the related rhodium-catalyzed reaction of vinylarenes also occurs with arylaluminum leading to stilbene derivatives.[11-13] During the course of our studies on such reactions, we have observed several unexpected findings that the reaction of diethyl(phenyl)aluminum (**1a**) with styrene resulted in affording exceeding amounts of *trans*-stilbene (**2a**) to the stoichiometry of the employed styrene. When the reaction of styrene with diethyl(4-methylphenyl)aluminum (**1b**) was performed, unexpected (*E*)-1,2-bis(4-methylphenyl)ethane (**2b**) was obtained along with desired (*E*)-1-(4-methylphenyl)-2-phenylethene (**2ab**). No such byproduct was found to afford in the reaction of aluminum reagent bearing methyl substituent, instead. (Scheme 1)

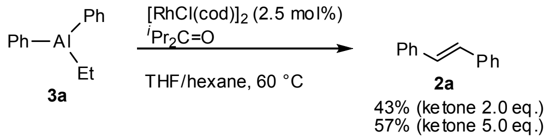


Scheme 1. Unexpected reaction of aryl(diethyl)aluminum

These findings suggest that the two carbon units in styrene are derived from the ethyl group of **1a** to induce double Mizoroki-Heck-type reaction to afford diarylethene **2**. Herein, we describe that *two mol amounts of aluminum aryls and ethylaluminum species form stilbene derivatives with a rhodium catalyst*, in which the ethyl group of aluminum serves as a ethylene source of stilbene.

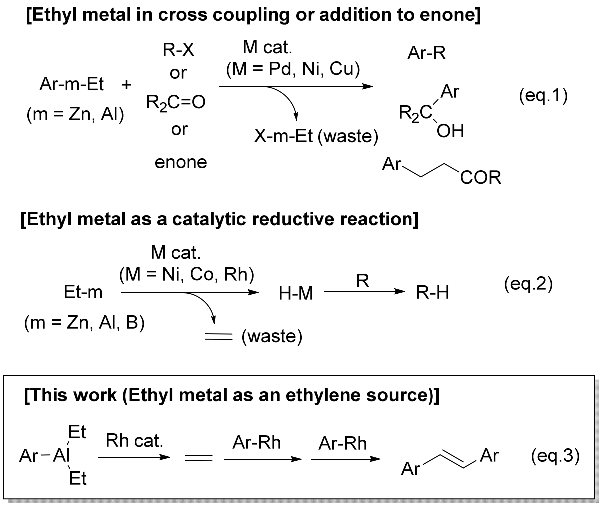
When diethyl(phenyl)aluminum (**1a**) was treated with 2.5 mol % $[RhCl(cod)]_2$ (5 mol % of Rh) in the presence of diisopropyl ketone (2 eq), 76% of *trans*-stilbene (**2a**) was obtained after stirring in THF at 60 °C, whereas no reaction took place in the absence of diisopropyl ketone.[11] The reaction of ethyl(diphenyl)aluminum **3a**, which was obtained by the reaction of ethylaluminum dichloride with 2.0 equivalents of PhMgX, also afforded **2a** in 43% yield under similar conditions. The yield was found to improve to 57% when the amount of ketone employed was increased to 5.0 equivalents.





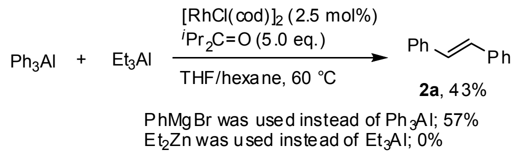
Scheme 2. Rhodium catalyzed reaction of diethyl(phenyl)aluminum

Concerning the transition metal-catalyzed reactions with main group organometallics such as zinc, aluminum, silicon, and tin, metal alkyl species have been recognized as dummy substituents, which are hardly introduced into the component of the target molecule as shown in Scheme 3 (eq 1).[14] Although the alkyl group of main group organometallics are shown to induce β-hydride elimination to give the corresponding metal hydride in the presence or absence of transition metals, to serve as a reducing agent for unsaturated bonds or organic halides, the thus produced olefinic species has only been served as a waste molecule.[15] (eq 2) Worthy of note in the present rhodium-catalyzed reaction with ethylaluminum is that the reaction shows unprecedented utilization of the ethyl group as an ethylene source as shown in eq 3.



Scheme 3 Ethyl-metal species in organometallic reactions

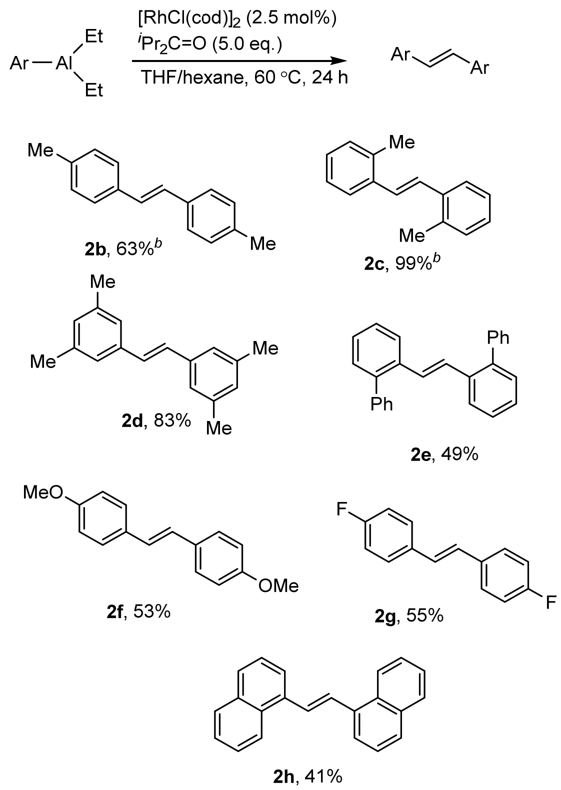
Both aryl and ethyl groups present in the same molecule is not the requirement in the rhodium-catalyzed stilbene synthesis. The use of triethylaluminum (Et_3Al) as an ethyl source with triphenylaluminum (Ph_3Al) in the presence of ketone and rhodium catalyst also afforded stilbene in 43% yield. In addition, the reaction with phenylmagnesium bromide (PhMgBr) instead of Ph_3Al afforded **2a** in 57% yield, whereas the use of diethylzinc (Et_2Zn) and Ph_3Al did not undergo the reaction at all. These reactions suggest that it is essential to use ehtylaluminum species to serve as an ethylene source of stilbene synthesis, while other arylmetallic species than aluminum allow the rhodium-catalyzed reaction.



Scheme 4. The reaction of triethylaluminum with triphnylaluminum

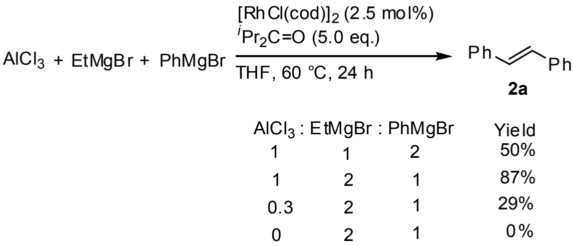
Table 1 summarized rhodium-catalyzed reaction of various arylated diethylaluminum. The reaction of 4-methylphenyl substituted diethylaluminum with rhodium catalyst and ketone took place to give dimethylstilbene **2b** in 63% yield. The reaction of 2-methylphenyl or 3,5-dimethylphenyl substituted diethylaluminum also proceeded to give the corresponding stilbene derivative **2c** and **2d** in excellent yields. Biphenyl or 1-naphthyl diethylaluminum also reacted in the presence of rhodium catalyst and ketone to give **2e** or **2h**. The use of diethylaluminum with methoxy group as an electron-donating group afforded **2f** in 53% yield. The reaction of diethyl(4-fluorophenyl)aluminum proceeded to furnish **2g** in 55% yield.

Table 1. Rhodium-catalyzed coupling reaction of various arylated diethylaluminum[a]



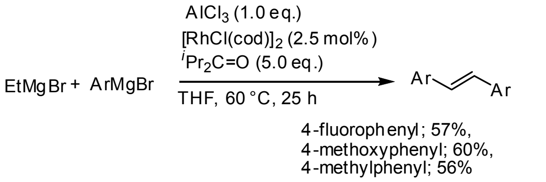
[a]Unless otherwise noted, the reaction was performed with aryl(diethyl)aluminum (0.5 mmol), ketone (2.5 mmol) and rhodium catalyst (0.0125 mmol) at 60 ºC for 24 h. [b] The reaction was carried out with 1.0 mmol of aryl(diethyl)aluminum and 2.0 mmol of ketone.

Combined use of ethyl and aryl Grignard reagent in the presence of aluminum chloride was also examined as shown in Scheme 5. The reaction was carried out with several different ratio of EtMgBr, PhMgBr, and $AlCl_3$. When the twice amounts of PhMgBr was employed toward EtMgBr and $AlCl_3$, the reaction occurred to furnish **2a** in 50% yield in the presence of rhodium catalyst (5.0 mol %) and diidopropyl ketone (5.0 eq.). The reaction of $AlCl_3$, EtMgBr and PhMgBr in 1:2:1 ratio improved the yield to 87% to afford **2a**. However, reducing the amount of $AlCl_3$ (30 mol%) to catalytic toward Grignard reagents resulted in giving 29% of **2a** and the reaction with Grignard reagent in the absence of $AlCl_3$ did not produce stilbene at all.[12] Although the stilbene synthesis only proceeds based on the employed amount of aluminum species, it is remarkable that the reaction with readily available Grignard reagents and $AlCl_3$ induces formation of both aryl and ethyl aluminum species in situ.



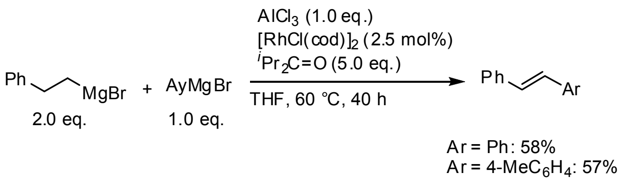
Scheme 5. The reaction of aluminum chloride and Grignard reagents leading to stilbene

Such combined use of $AlCl_3$ and Grignard reagent was then employed for several 1,2-diarylethenes as shown in Scheme 6. The reaction of (4-fluorophenyl)magnesium bromide occurred to afford the product in 57% yield. Other aryl Grignard reagents, 4-methylphenyl or 4-methoxyphenyl, also reacted to deliver stilbene derivatives in 56% and 60%, respectively.



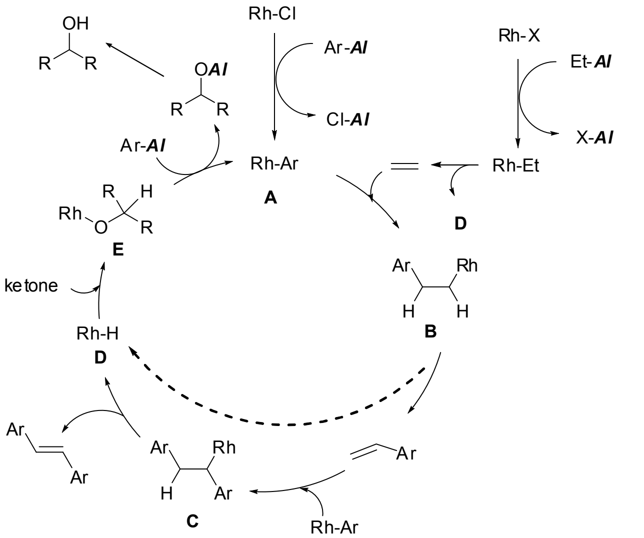
Scheme 6. Rhodium-catalyzed reaction of various ArMgX with EtMgBr and $AlCl_3$.

Although we have also attempted several metal alkyl species such as n-propyl, isobutyl, etc. instead of ethyl group, the reaction was found mostly unsuccessful to result in giving no desired addition-elimination product. However, the reaction bearing 2-phenethyl substituent took place smoothly. Treatment of (2-phenylethyl)magnesium bromide bearing β-hydrogen with aryl Grignard reagent in the presence of aluminum chloride afforded stilbene derivatives in 57-58% yields.



Scheme 7. Reaction of 2-phenylethyl metal reagent as a styrene source

A plausible reaction mechanism is shown in scheme 8. Transmetalation reactions of both ethyl and aryl groups of aluminum species to rhodium afford arylrhodium **A** and ethylated rhodium species. The ethylated rhodium immediately induce β-hydride elimination to release ethylene along with formation of hydridorhodium. Insertion of ethylene to the thus formed carbon-rhodium bond of arylrhodium species **A** leads to the addition product **B**, which undergoes β-hydride elimination to give styrene. Since formation of styrene has been hardly observed throughout the present rhodium-catalyzed reactions, the generated styrene reacts with arylrhodium **A** much faster than ethylene to form **C**. Beta-hydride elimination of **C** affords stilbene accompanied by formation of rhodium hydride **D**. Ketone was reduced by **D** to furnish rhodium alkoxide **E**, which is capable of undergoing transmetalation of arylaluminum to regenerate arylrhodium complex **A**.[16]



Scheme 8. Plausible mechanism of 1,2-diarylethene synthesis

In conclusion, we have shown that ethyl group of aluminum species serves as an ethylene source in rhodium-catalyzed stilbene synthesis. The reaction proceeded in the presence of diisopropyl ketone and the rhodium catalyst to give *trans*-stilbene in good to excellent yields. The reaction can be recognized as a novel class of incorporation of a small molecule surrogate employed as a metal-alkyl species into the organic framework. The reaction proceeded using organoaluminum reagent bearing ethyl and aryl groups as well as combined use of ArMgX, EtMgX, and aluminum chloride, which merits procedural simplicity.

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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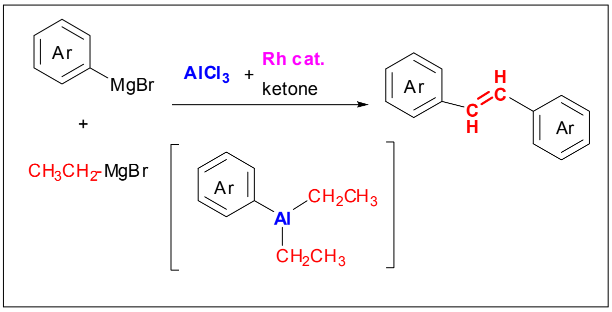
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