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Ethylaluminum as an ethylene source for the Mizoroki–Heck-type reaction. Rhodium-catalyzed preparation of stilbene derivatives†

Shota Tanaka, Kazuki Itami, Kazuhiro Sunahara, Go Tatsuta and Atsunori Mori*

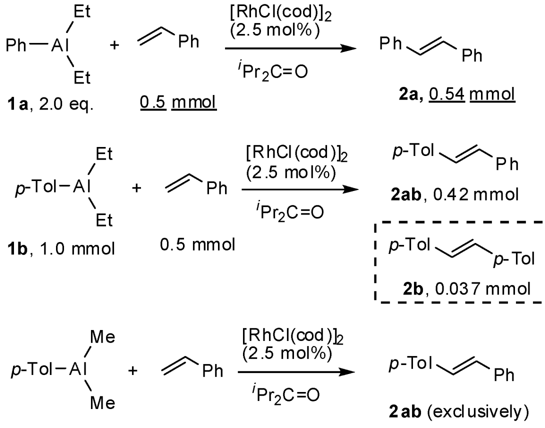
Treatment of an organoaluminum reagent bearing aryl and ethyl groups furnishes 1,2-diarylethene derivatives in good to excellent yields by the catalysis of a rhodium complex, in which the ethyl group of the aluminum reagent serves as an ethylene source in the product formation.

Incorporation of small molecules such as carbon monoxide, carbon dioxide, hydrogen, nitrogen, oxygen, *etc.* into organic compounds is an attractive approach for the functionalization of the organic framework in organic synthesis. Transition metals as catalysts play a key role in 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 a CO source, *etc.*[2] Several metallic alkyls have also been employed as synthetic equivalents of the metal hydrides for the reduction of carbonyl compounds through β-hydride elimination accompanied by the formation of the corresponding olefins.[3] Compared with the use of metal alkyls as reducing agents as hydrides, little attention has been paid so far to the produced olefins as building blocks of organic compounds.[4]

On the other hand, reactions using rhodium catalysts have been widely used as essential tools in forming a variety of C–C bonds in organic synthesis.[5] In particular, various reactions using organometallic species (boron, silane, zinc, tin, aluminum, *etc.*) as nucleophiles, such as cross coupling with organic halides,[6] conjugated addition to enones,[7] 1,2-addition to carbonyl compounds,[8] and the 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 olefins in the presence of a rhodium or an 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 observed several unexpected findings: the reaction of diethyl(phenyl)aluminum (**1a**) with styrene afforded 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 in the reaction of an aluminum reagent bearing a methyl substituent, instead (Scheme 1).

These findings suggest that the two carbon units in styrene are derived from the ethyl group of **1a** to induce the 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 using a rhodium catalyst*, in which the ethyl group of aluminum serves as an ethylene source in stilbene synthesis.

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



Scheme 1 Unexpected reaction of aryl(diethyl)aluminum.

Department of Chemical Science and Engineering, Kobe University, 1-1 Rokkodai, Nada, Kobe 657-8501, Japan. E-mail: amori@kobe-u.ac.jp; Fax: +81-78-803-6181; Tel: +81-78-803-6181

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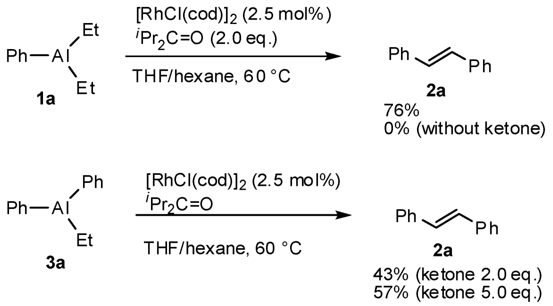
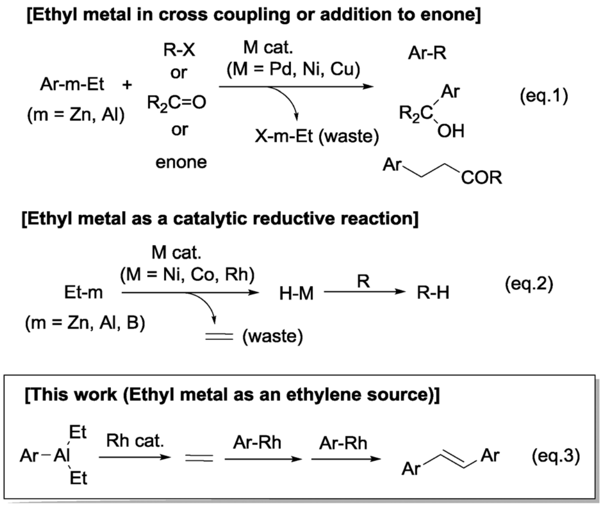


Scheme 2 Rhodium catalyzed reaction of diethyl(phenyl)aluminum.

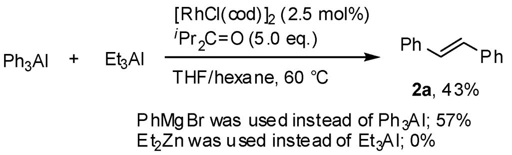
THF/hexane at 60 °C, whereas no reaction took place in the absence of diisopropyl ketone.[11] The reaction of ethyl(diphenyl)-aluminum **3a**, which was obtained by the reaction of ethylaluminum dichloride with 2.0 equivalents of PhMgX, also afforded **2a** in 43% yield under similar conditions. The yield was found to improve to 57% when the amount of ketone employed was increased to 5.0 equivalents (Scheme 2).

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 (eqn (1)).[14] Although the alkyl groups of main group organometallics are shown to induce β-hydride elimination to give the corresponding metal hydrides in the presence or absence of transition metals, to serve as reducing agents for unsaturated bonds or organic halides, the thus produced olefinic species have only served as waste molecules[15] (eqn (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 eqn (3).

The presence of both aryl and ethyl groups 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 the ketone and a rhodium catalyst also afforded stilbenes 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 allow the reaction to proceed at all. These reactions suggest that it is essential to use ethylaluminum species to serve as an ethylene source in stilbene synthesis, while arylmetallic species other than aluminum allow the rhodium-catalyzed reaction to occur (Scheme 4).



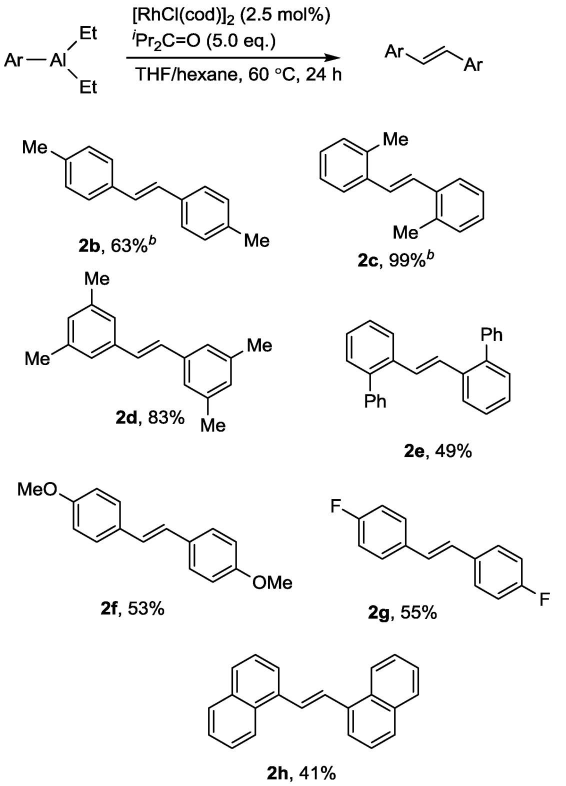
Scheme 3 Ethyl-metal species in organometallic reactions.



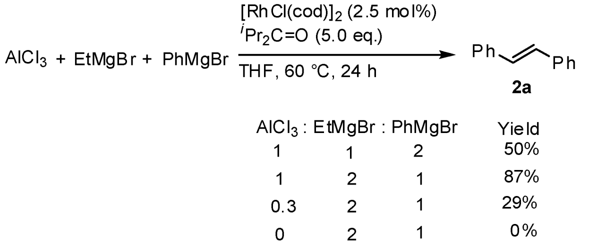
Scheme 4 The reaction of triethylaluminum with triphenylaluminum.

Table 1 summarizes the rhodium-catalyzed reaction of various arylated diethylaluminum. The reaction of 4-methylphenyl substituted diethylaluminum with the 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 derivatives **2c** and **2d** in excellent yields. Biphenyl or 1-naphthyl diethylaluminum also reacted in the presence of the rhodium

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 a rhodium catalyst (0.0125 mmol) at 60 °C for 24 h. [b] The reaction was carried out with 1.0 mmol of aryl(diethyl)aluminum and 2.0 mmol of ketone.



AlCl$_3$	EtMgBr	PhMgBr	Yield
1	1	2	50%
1	2	1	87%
0.3	2	1	29%
0	2	1	0%

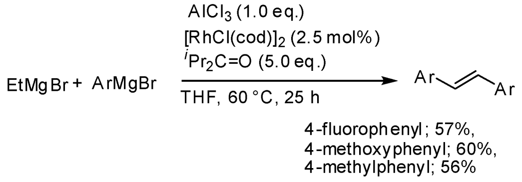
Scheme 5 The reaction of aluminum chloride and Grignard reagents leading to stilbene.

catalyst and ketone to give **2e** or **2h**. The use of diethylaluminum with the 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.

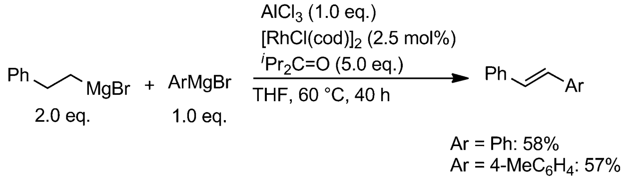
The combined use of ethyl and aryl Grignard reagents in the presence of aluminum chloride was also examined, as shown in Scheme 5. The reaction was carried out with several different ratios of EtMgBr, PhMgBr, and AlCl$_3$. When double the amount of PhMgBr was employed toward EtMgBr and AlCl$_3$, the reaction occurred to furnish **2a** in 50% yield in the presence of a rhodium catalyst (5.0 mol%) and diisopropyl ketone (5.0 eq.). The reaction of AlCl$_3$, EtMgBr and PhMgBr in a 1 : 2 : 1 ratio improved the yield to 87% to afford **2a**. However, reducing the amount of AlCl$_3$ (30 mol%) to catalytic amounts toward Grignard reagents afforded 29% of **2a** and the reaction with the Grignard reagent in the absence of AlCl$_3$ did not produce stilbenes 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 the formation of both aryl and ethyl aluminum species *in situ*.

This combined use of AlCl$_3$ and Grignard reagents 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 and 4-methoxyphenyl, also reacted to deliver stilbene derivatives in 56% and 60% yields, respectively.

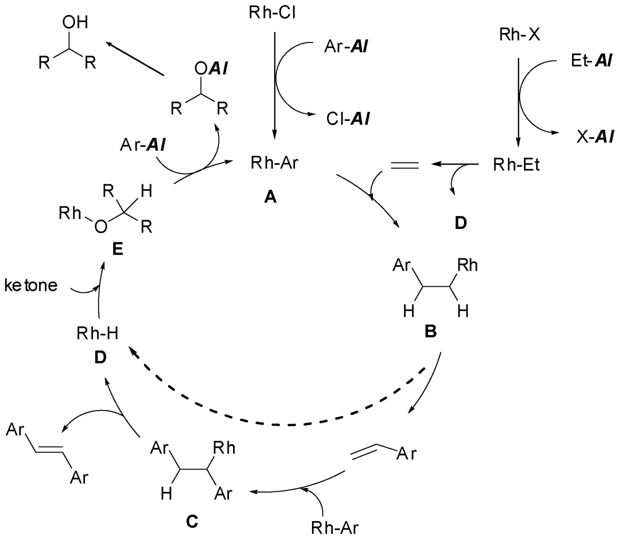
Although we also used several metal alkyl species such as *n*-propyl, isobutyl, *etc.* instead of an ethyl group, the reaction was mostly found to be unsuccessful in giving the desired addition-elimination product. However, the reaction bearing the 2-phenethyl substituent took place smoothly. Treatment of (2-phenylethyl)magnesium bromide bearing β-hydrogen with aryl Grignard reagents in the presence of aluminum chloride afforded stilbene derivatives in 57–58% yields (Scheme 7).



Scheme 6 Rhodium-catalyzed reaction of various ArMgX with EtMgBr and AlCl$_3$.



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



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

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 the ethylated rhodium species. The ethylated rhodium immediately induces β-hydride elimination to release ethylene along with the 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 the formation of rhodium hydride **D**. The ketone was reduced by **D** to furnish rhodium alkoxide **E**, which is capable of undergoing transmetalation of arylaluminum to regenerate arylrhodium complex **A**.[16]

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

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