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Carborhodation

Rhodium-Catalyzed Rearrangement of Aryl Bis(alkynyl) Carbinols to 3-Alkynyl-1-indanones**

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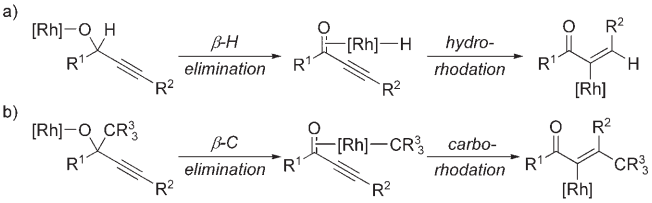
A transition-metal-catalyzed isomerization or rearrangement can provide an efficient way to convert readily accessible organic compounds into those with more structural complexity under mild conditions.[1] For example, rhodium-catalyzed isomerization of secondary propargyl alcohols to the corresponding α,β-unsaturated ketones was described,[2] and a reaction pathway involving β-hydrogen elimination of an alkoxorhodium species with subsequent hydrorhodation of an alkyne was proposed (Scheme 1 a).[2b] This reaction sequence was applied to the synthesis of 1-indanones by employing α-aryl propargyl alcohols.[3] In contrast, an analogous process with tertiary propargyl alcohols involving β-carbon elimination[4] and successive carborhodation has yet to be reported (Scheme 1 b).[5] Within this context we describe the development of a rhodium-catalyzed rearrangement of readily available aryl bis(alkynyl) carbinols to 3-alkynyl-1-indanones under mild conditions.



Scheme 1. a) Proposed reaction pathway for the rhodium-catalyzed isomerization of secondary propargyl alcohols; b) possible reaction pathway for the potential rhodium-catalyzed rearrangement of tertiary propargyl alcohols.

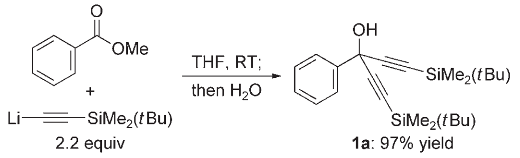


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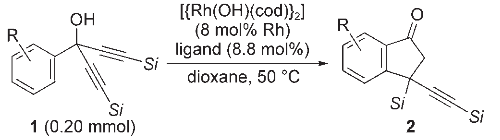
Table 1: Rhodium-catalyzed rearrangement of **1** to indanones **2**.



Entry	Substrate	Ligand	Product	Yield [%][a]
1	**1a** (R = H, *Si* = SiMe$_2$(*t*Bu))	none	**2a**	(5)
2[b]	**1a**	PPh$_3$	**2a**	(19)
3	**1a**	dppb	**2a**	(9)
4	**1a**	dppp	**2a**	(45)
5	**1a**	binap	**2a**	73
6[c]	**1a**	binap	**2a**	79
7	**1b** (R = H, *Si* = SiEt$_3$)	binap	**2b**	63
8	**1c** (R = H, *Si* = Si(*n*Pr)$_3$)	binap	**2c**	66
9	**1d** (R = 2-Me, *Si* = SiMe$_2$(*t*Bu))	binap	**2d**	85
10	**1e** (R = 4-Me, *Si* = SiMe$_2$(*t*Bu))	binap	**2e**	71
11	**1f** (R = 4-OMe, *Si* = SiMe$_2$(*t*Bu))	binap	**2f**	87
12	**1g** (R = 4-F, *Si* = SiMe$_2$(*t*Bu))	binap	**2g**	85
13	**1h** (R = 4-Cl, *Si* = SiMe$_2$(*t*Bu))	binap	**2h**	84

[a] Yield of isolated product. Numbers in parentheses were determined by using ^{1}H NMR spectroscopy with an internal standard (MeNO$_2$). [b] 16 mol% of ligand was used. [c] The reaction was conducted on a 5.0 mmol scale.

Initially, we prepared phenyl bis((*tert*-butyldimethylsilyl)ethynyl) carbinol (**1a**) as a model substrate [Eq. (1)] and treated it with [{Rh(OH)(cod)}$_2$] (8 mol% Rh) at 50 °C (Table 1, entry 1). Under these conditions indanone **2a** was obtained in only 5% yield. The use of PPh$_3$ as a ligand gave a somewhat better yield (19%) of **2a** (Table 1, entry 2), and use of dppb as the ligand resulted in a low yield of 9% (Table 1, entry 3). In both cases the major component after the reaction was unreacted **1a**. In contrast, the yield of **2a** was improved by using other bisphosphine ligands such as dppp and binap, giving a 45% yield (Table 1, entry 4) and a 73% yield (Table 1, entry 5), respectively. The present reaction of **1a** can be easily scaled up to 5 mmol, and leads to 79% yield of **2a** (Table 1, entry 6). Under the reaction conditions using binap as the ligand, substrates derived from triethylsilyl- and tri-*n*-propylsilylacetylenes (**1b** and **1c**) also underwent the rearrangement to give indanones **2b** and **2c**, respectively (63–66% yield; Table 1, entries 7 and 8). In addition, various substituents on the aromatic ring of the substrate were tolerated, giving the corresponding indanones in high yield (71–87% yield; Table 1, entries 9–13).[6]

A proposed catalytic cycle of this process is illustrated in Scheme 2. Alkoxorhodium species **A**, which is initially

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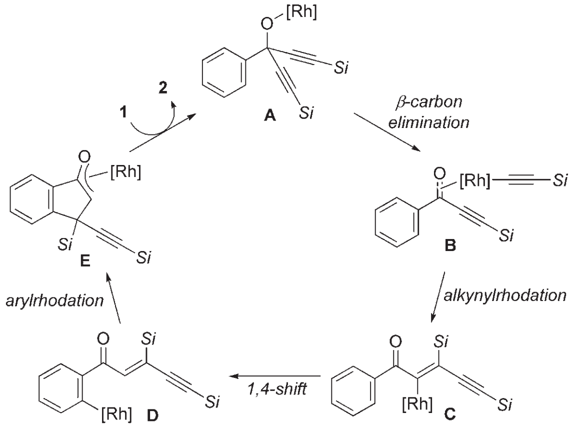
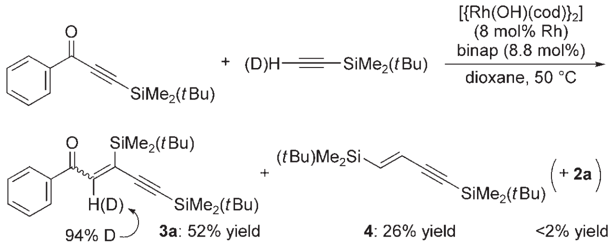


Scheme 2. Proposed catalytic cycle of the rhodium-catalyzed rearrangement of **1** to **2**. [Rh] = Rh(binap), *Si* = Si(alkyl)$_3$.

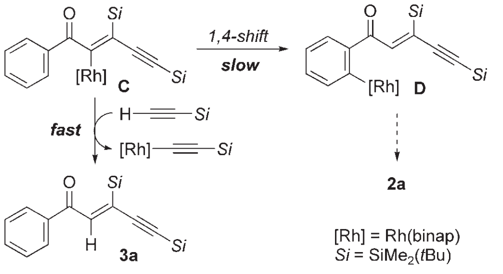
generated from the hydroxorhodium catalyst and substrate **1a**, undergoes β-alkynyl elimination to give intermediate **B**.[7] Alkynylrhodation of **B** to the conjugated alkyne generates alkenylrhodium species **C** with subsequent 1,4-rhodium migration to form arylrhodium intermediate **D**.[3,8] This intermediate undergoes intramolecular 1,4-addition (arylrhodation) to give oxa-π-allylrhodium **E** with subsequent protonolysis by alcohol **1** to produce indanone **2** and regenerate alkoxorhodium **A**.

It is worth comparing the present rearrangement with an intermolecular reaction between an aryl alkynyl ketone and a terminal alkyne,[9] which in principle can also provide the same 3-alkynyl-1-indanone as the product.[8d,e] In reality, however, a reaction of 3-(*tert*-butyldimethylsilyl)-1-phenyl-2-propyn-1-one with (*tert*-butyldimethylsilyl)acetylene in the presence of a Rh/binap catalyst gave almost no indanone **2a** and the major products were uncyclized conjugated ynenone **3a** (52% yield) and alkyne dimer **4** (26% yield) [Eq. (2)].[10]



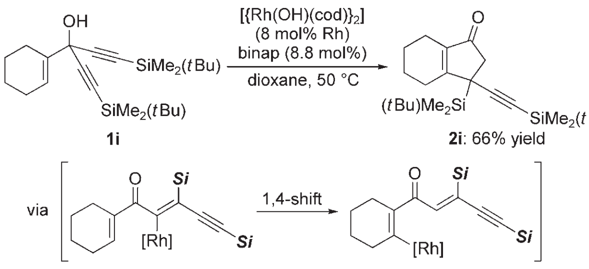
(2)

The use of deuterated (*tert*-butyldimethylsilyl)acetylene in this reaction revealed that the deuterium was mostly incorporated at the alkenyl carbon atom adjacent to the carbonyl group of product **3a**. This result indicates that the ligand exchange between alkenylrhodium intermediate **C** and a terminal alkyne occurs faster than the 1,4-rhodium migration from **C** to **D**, suppressing the subsequent formation of indanone **2a** (Scheme 3, see also Scheme 2). Because a free terminal alkyne does not exist in the rearrangement of aryl bis(alkynyl) carbinols, our newly developed catalysis has a significant advantage for the efficient synthesis of 3-alkynyl-1-indanones.



Scheme 3. Proposed reaction pathway for the formation of **3a**.

The same mode of rearrangement is also observed with substrate **1i** which has 1-cyclohexenyl group at the bis(propargylic) position, giving cyclopentenone derivative **2i** in 66% yield [Eq. (3)]. This outcome represents a rare example



(3)

that involves 1,4-rhodium migration from an alkenyl carbon atom to another alkenyl carbon atom.

In summary, we have developed a rhodium-catalyzed rearrangement of aryl bis(alkynyl) carbinols to 3-alkynyl-1-indanones through a pathway involving a β-carbon elimination/carborhodation sequence under mild conditions. Considering the ease of the synthesis of carbinol substrates from an aromatic ester and a terminal alkyne in a single step, the present catalysis provides an efficient way of preparing 3-alkynyl-1-indanones.

Experimental Section

General procedure for Table 1: A solution of [{Rh(OH)(cod)}$_2$] (3.6 mg, 16 μmol Rh) and ligand (18 μmol) in 1,4-dioxane (3.0 mL) was stirred for 20 min at room temperature. Compound **1** (0.20 mmol) was added with additional 1,4-dioxane (2.0 mL) and the mixture was stirred for 48 h at 50 °C. The reaction was quenched with water and extracted with Et$_2$O. The organic layer was dried over MgSO$_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel preparative TLC with EtOAc/hexanes to afford product **2**.

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