Communication

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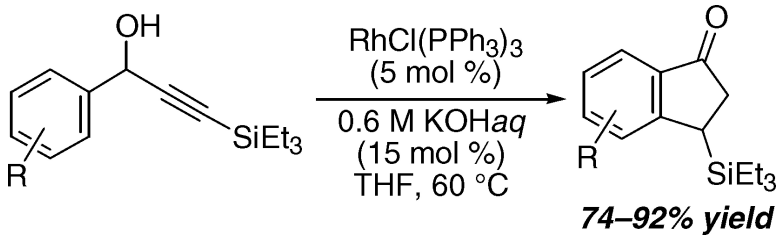

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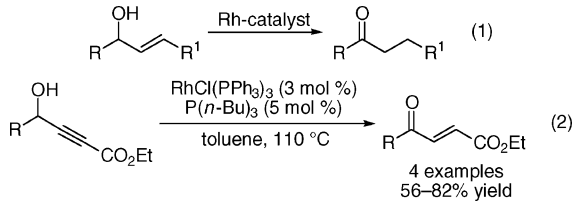
Rhodium-Catalyzed Isomerization of α-Arylpropargyl Alcohols to Indanones: Involvement of an Unexpected Reaction Cascade

Ryo Shintani, Kazuhiro Okamoto, and Tamio Hayashi*

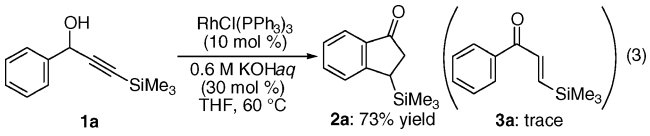
Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

Received December 10, 2004; E-mail: thayashi@kuchem.kyoto-u.ac.jp

Transition-metal-catalyzed isomerization of organic compounds can provide unique opportunities that are not easily accessible by conventional thermal processes.[1] For example, rhodium-catalyzed isomerizations of allylic alcohols are well-known transformations that effectively provide the corresponding saturated carbonyl compounds (eq 1).[1c] On the other hand, little progress has been described for the isomerization of propargyl alcohols to α,β-unsaturated carbonyl compounds under rhodium catalysis. In fact, to the best of our knowledge, only one report has addressed this issue to date, a study by Pellicciari that focused on the reaction of propargyl alcohols directly attached to an ester in the presence of $RhCl(PPh_3)_3/P(n\text{-}Bu)_3$ at 110 °C (eq 2).[2,3] In this Communication, we describe our new findings in the context of propargyl alcohol isomerizations, that is, α-arylpropargyl alcohols are isomerized to indanones in the presence of a rhodium catalyst under mild conditions. We also demonstrate our mechanistic investigations, proposing the catalytic cycle of this process.



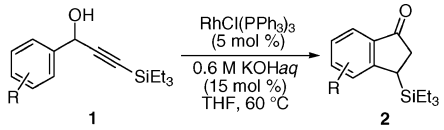
Initially, we employed propargyl alcohol **1a** as a model substrate in the presence of 10 mol % Wilkinson's catalyst in THF at 60 °C (eq 3), expecting that it might generate the corresponding α,β-enone (**3a**). To our surprise, the ^{1}H NMR analysis of the crude reaction mixture revealed that only a trace amount of **3a** was detected, and most of the material was converted to another compound, which was identified as indanone **2a** upon chromatographic purification (73% isolated yield).

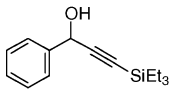
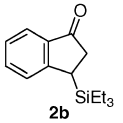
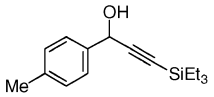
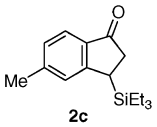
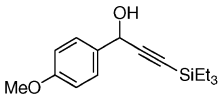
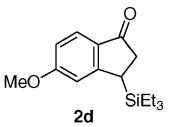
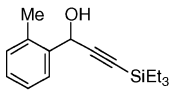
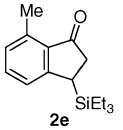
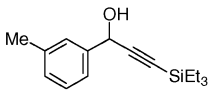
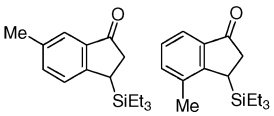
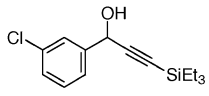
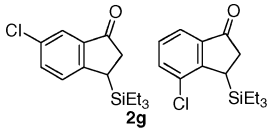


After some investigations, we found that the reaction also proceeds with 5 mol % catalyst loading, and the triethylsilyl group is more robust than the trimethylsilyl group under these reaction conditions.[4] As shown in Table 1, substrates with a variety of substitution patterns on the aromatic ring effectively undergo the isomerization to furnish the corresponding indanones in good to excellent yields (74−92% yield). It is worth noting that the cyclization occurs selectively at the less hindered site of the aromatic ring when meta-substituted substrates are employed (≥10/1 selectivity; entries 5 and 6).

To probe the mechanism of these isomerization reactions, we employed deuterium-labeled substrates (eqs 4 and 5). These

Table 1. Rhodium-Catalyzed Isomerization of 1-Aryl-3-triethylsilyl-2-propyn-1-ols: Scope



entry	substrate	product	yield (%)
1	 **1b**	 **2b**	92
2	 **1c**	 **2c**	87
3	 **1d**	 **2d**	90
4	 **1e**	 **2e**	84
5[a]	 **1f**	 **2f**	76 (>20/1)
6[a]	 **1g**	 **2g**	74 (10/1)

[a] Using 10 mol % catalyst.

experiments revealed that the methyne proton of the alcohol ends up at the β-position of the indanone (>98% D; eq 4), whereas the ortho-proton of the phenyl group is shifted to the α-position (89% D at 26% conversion; eq 5).[5] On the basis of the outcome of these studies, a proposed catalytic cycle of this process is depicted in Figure 1. Thus, a formation of an alkoxorhodium species by the ligand exchange between a hydroxorhodium[6] and the propargyl alcohol, followed by the β-hydrogen elimination, generates a hydrido(alkynone) rhodium intermediate (**A**). This, then, undergoes a conjugate hydrorhodation, followed by a 1,4-hydrogen shift, and affords an arylrhodium intermediate (**B**).[7] An intramolecular 1,4-addition of this intermediate, followed by hydrolysis,[8] provides the final product, indanone, and regenerates the hydroxorhodium species. As part of the further support of this proposed cycle, we conducted a stoichiometric reaction using alkynone **6** with

10.1021/ja042582g CCC: $30.25

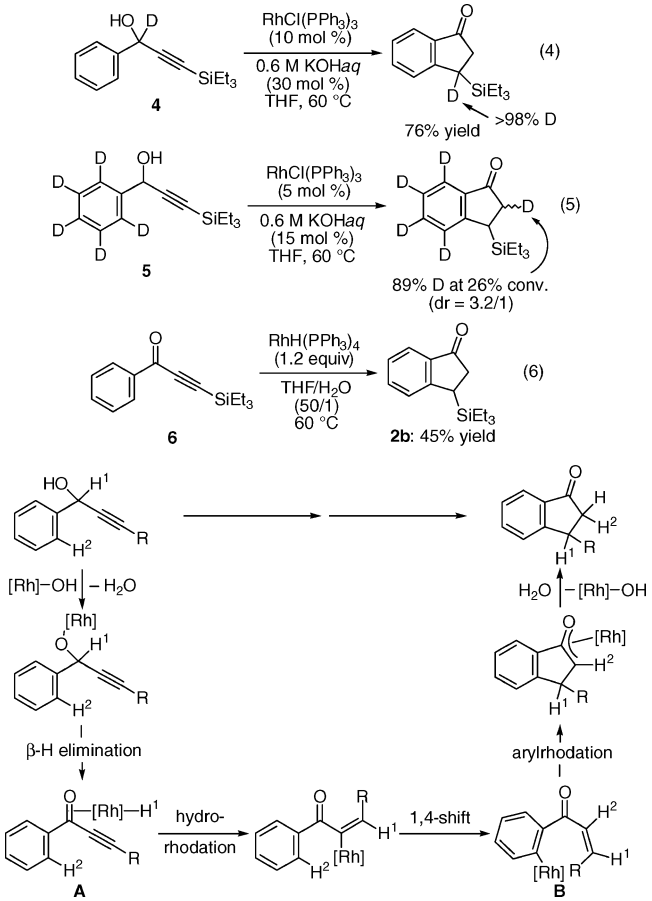
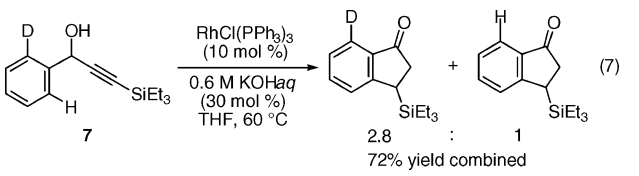


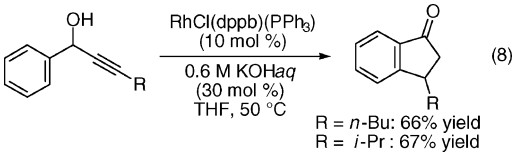
Figure 1. Proposed catalytic cycle of the rhodium-catalyzed isomerization of α-arylpropargyl alcohols.

$RhH(PPh_3)_4$ (eq 6), which gave indanone **2b** in 45% yield (not optimized), indicating the feasibility of the intermediacy of alkynone **A** in Figure 1.[9]

We also carried out a series of competition experiments as follows to gain more insights. (1) When a 1:1 mixture of **1b** and **4** was subjected to the isomerization reaction, both **1b** and **4** reacted in the same rate ($k_H/k_D = 1.0$),[10,11] and (2) when a 1:1 mixture of **1b** and **5** was employed, these reacted almost in the same rate with each other as well ($k_H/k_D = 1.1$).[12] In addition, (3) the reaction with monodeuterated substrate **7** provided the corresponding indanone with 74% D at the ortho-carbon of the benzene ring, showing that the reaction proceeded with $k_H/k_D = 2.8$ (eq 7). These results indicate that the 1,4-hydrogen shift (formation of **B** in Figure 1) is the turnover-limiting step of the catalytic cycle, and that there is an irreversible step (presumably the step of conjugate hydrorhodation to intermediate **A** in Figure 1) prior to this 1,4-shift because an intermolecular competition between **1b** and **5** shows almost no difference in reactivity with each other.



Unfortunately, the catalytic isomerization conditions using Wilkinson's catalyst are not very effective for propargyl alcohols bearing an alkyl group, instead of a silyl group on the alkyne, which tend to give a complex mixture of multiple products. After examining various catalysts,[13] however, we were able to find that $RhCl(dppb)(PPh_3)$ catalyzes the isomerization of alkylacetylene-derived propargyl alcohols to the corresponding indanones in relatively high yields (66−67% yield; eq 8).



In summary, we have developed a rhodium-catalyzed isomerization of α-arylpropargyl alcohols to indanones under mild conditions. Considering the ease of preparation of these substrates (terminal alkynes + aromatic aldehydes), this method provides a new way of constructing indanones with high efficiency. In addition, by the mechanistic investigations using deuterium-labeled substrates, we have disclosed that the reaction goes through an unexpected cascade, with a 1,4-hydrogen shift being the turnover-limiting step of the catalytic cycle.

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Supporting Information Available: Experimental procedures and compound characterization data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(2) Saïah, M. K. E.; Pellicciari, R. *Tetrahedron Lett.* **1995**, *36*, 4497.
(3) Several examples of propargyl alcohol isomerizations catalyzed by other transition metals have been reported. Ruthenium catalysis: (a) Trost, B. M.; Livingston, R. C. *J. Am. Chem. Soc.* **1995**, *117*, 9586. (b) Ma, D.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1989**, 890. (c) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Tetrahedron Lett.* **2002**, *43*, 7531. Iridium catalysis: (d) Ma, D.; Lu, X. *Tetrahedron Lett.* **1989**, *30*, 2109. Palladium catalysis: (e) Lu, X.; Ji, J.; Guo, C.; Shen, W. *J. Organomet. Chem.* **1992**, *428*, 259. (f) Guo, C.; Lu, X. *Synlett* **1992**, 405. Rhenium catalysis: (g) Narasaka, K.; Kusama, H.; Hayashi, Y. *Tetrahedron* **1992**, *48*, 2059. See also: (h) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (i) Harrak, Y.; Blaszykowski, C.; Bernard, M.; Cariou, K.; Mainetti, E.; Mouriès, V.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2004**, *126*, 8656.
(4) In some cases, we have obtained partially desilylated indanones when trimethylsilyl-substituted substrates are used.
(5) Due to the basic aqueous media, an H−D exchange at the α-position occurs to lower the D-content at higher conversions.
(6) Treatment of a chlororhodium complex with aqueous KOH is known to produce a hydroxorhodium species. For examples, see: (a) Grushin, V. V.; Kuznetsov, V. F.; Bensimon, C.; Alper, H. *Organometallics* **1995**, *14*, 3927. (b) Uson, R.; Oro, L. A.; Cabeza, J. A. *Inorg. Synth.* **1985**, *23*, 126.
(7) For examples of a formation of an arylrhodium species involving a 1,4-hydrogen shift, see: (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918. (b) Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464.
(8) In an intermolecular system, we reported a mechanism involving a formation of an oxa-π-allylrhodium complex by the addition of a phenylrhodium species to an enone and its hydrolysis to give a hydroxorhodium complex and a 1,4-addition product: Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.
(9) Under the catalytic reaction conditions, *trans*-1-phenyl-3-triethylsilyl-2-propen-1-one (**3b**) does not produce indanone **2b**, thereby eliminating the possibility of a Nazarov-cyclization mechanism.
(10) Determined by ^{1}H NMR at 6% conversion.
(11) For a recent example of an intermolecular kinetic isotope effect study using ^{1}H NMR analyses, see: Adams, C. S.; Legzdins, P.; McNeil, W. S. *Organometallics* **2001**, *20*, 4939.
(12) Determined by ^{1}H NMR at 4% conversion.
(13) (a) The use of bisphosphine ligands, such as dppb and dppf, is particularly effective among those examined (dppe, messy reaction; dppp, low reactivity). (b) The use of $RhCl(bisphosphine)(PPh_3)$ gives cleaner reactions than the use of $[RhCl(bisphosphine)]_2$ (which usually results in the formation of rhodium-black).

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