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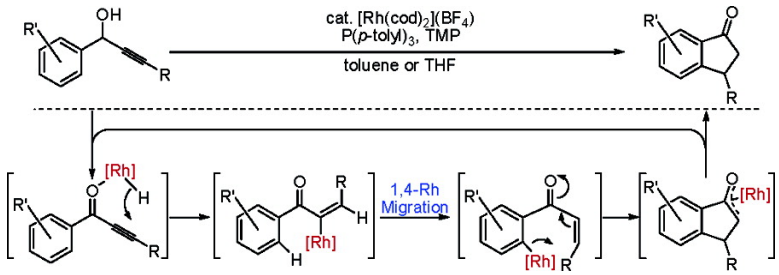
J. Am. Chem. Soc., **2005**, 127 (10), 3248-3249• DOI: 10.1021/ja042581o • Publication Date (Web): 16 February 2005



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Rh(I)-Catalyzed Cyclization of 1-Arylprop-2-yn-1-ol Derivatives Utilizing Rhodium 1,4-Migration

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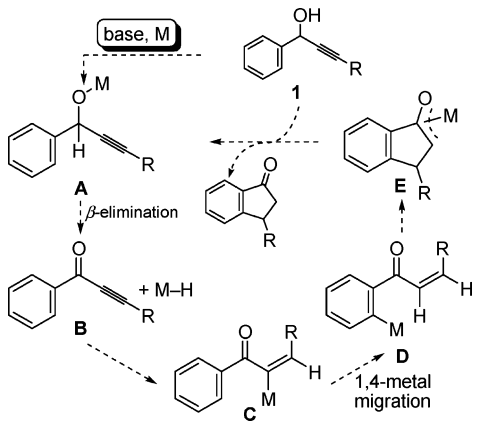
Construction of a cyclopentanone ring onto aromatic compounds is highly useful, as these bicyclic compounds have abundant use as synthetic intermediates.[1−4] The most direct method for this transformation is the intramolecular Friedel−Crafts acylation of 3-arylpropanoic acid derivatives;[2] however, this method usually necessitates the use of strong acids such as $AlCl_3$, CF_3SO_3H, and so forth, and is not easy to be applied for the heteroaromatic compounds. For example, pyridine derivatives are well-known to be resistant to standard Friedel−Crafts acylation conditions, and other heteroaromatics such as furan, thiophene, pyrrole, and indole derivatives have not been employed extensively compared with benzene derivatives.[5] Thus, it is desirable to develop a concise method for the formation of a cyclopentanone ring onto aromatic systems, which is applicable to various heteroaromatic compounds.

To carry out this process under mild conditions in a catalytic manner, we have designed the following reaction based on transition-metal-catalyzed intramolecular C−H bond activation (Scheme 1). Treatment of propargyl alcohols **1**, easily accessible via an addition of acetylides to the corresponding aryl aldehydes, with a certain transition-metal complex in the presence of a base would give alkoxo complexes **A**, which would give alkynyl ketones **B** and hydride complex (M−H) via β-hydride elimination. Successive hydrometalation[6] of the alkynyl ketones would give alkenylmetallic species **C**. Then, 1,4-metal migration would occur through the C−H insertion of the alkenylmetallic species to the ortho-position of the aryl group to give arylmetallic intermediates **D**.[7] Conjugate addition of the intermediates **D** would give enolates **E**,[8] which undergo proton exchange with the alcoholic substrate **1** to regenerate the alkoxo complex **A**.

On the basis of these considerations, we examined the reaction of propargyl alcohol **1a** with several transition-metal complexes in the presence of a base. Late transition metals such as Ru(II), Pt(II), and Ir(I)−phosphine complexes did not show the activity for this transformation.[9] Gratifyingly, treatment of **1a** with 10 mol % of $[Rh(cod)_2](BF_4)$ and 40 mol % of PPh_3 in the presence of 10 mol % of BuLi as a base at room temperature gave the desired indanone derivative **2a** in 36% yield (Table 1, entry 1). To optimize

Scheme 1



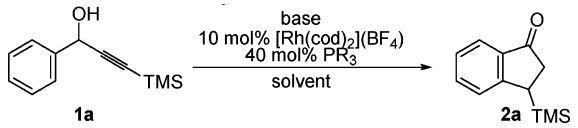


Table 1. Reaction of Propargyl Alcohol **1a**[a]

entry	PR_3	base (equiv)	temp (°C)	solvent	time	yield (%)
1	PPh_3	BuLi (0.1)	rt	toluene	14 d	36
2	PPh_3	TMP (1.0)	rt	toluene	7 d	40
3	PPh_3	TMP (1.0)	90	toluene	17 h	36
4	PCy_3	TMP (1.0)	90	toluene	14 h	N. R.
5	P(*p*-toyl)$_3$	TMP (1.0)	90	toluene	3 h	80
6	P(*p*-toyl)$_3$	TMP (1.0)	67	THF	4 h	86
7	P(*p*-toyl)$_3$	TMP (0.1)	67	THF	17 h	64

[a] TMP = 2,2,6-tetramethylpiperidine; rt = room temperature.

the reaction conditions, we examined the effect of the base and the phosphine, and the results are summarized in Table 1. Not only a strong base such as BuLi but also a weak base such as 2,2,6,6-tetramethylpiperidine (TMP) is employable in this reaction (entry 2). Higher temperature accelerated the reaction considerably (entry 3). As for the effect of the phosphine and the solvent, P(*p*-tolyl)$_3$ in either toluene or THF was found to be the most effective to give the cyclized product **2a** in 80 and 86% yield, respectively (entries 5 and 6), while alkyl phosphine did not promote the reaction at all (entry 4). Use of a catalytic amount of TMP retarded the reaction (entry 7).

The reactions of several substrates **1b** to **1k** were examined under the optimized conditions (Table 2). Not only electron-donating (entries 1 and 4) but also electron-withdrawing substituents (entry 2) on the phenyl ring were tolerated for this cyclization to give the corresponding indanone derivatives in good yield. The phenyl substituent on alkyne was also employable to give the cyclized product in moderate yield (entry 3). In the case of the reaction using naphthalene derivative **1f**, cyclopenta[b]naphthalene derivative **2f** was obtained as a major product, which is not easily available by the standard Friedel−Crafts reaction (entry 5). It is noteworthy that 3-pyridyl derivative **1g** also gave the cyclized product in 51% yield, which cannot be obtained by intramolecular Friedel−Crafts acylation due to the inherent basicity of the substrate (entry 6). Furthermore, substrates possessing a five-membered heteroaromatic ring can also be employed; reaction of 2-pyrrolyl-, 2-thienyl-, 3-thienyl-, and 1-(3-furyl)-prop-2-yn-1-ol derivatives all gave the corresponding cyclopentanones in moderate to good yield (entries 7−10).[10]

To elucidate the mechanism of this reaction, we next carried out a deuterium-labeling study. The reaction of deuterium-labeled **1a**-*d* (>98% *d* incorporated in the propargyl position) revealed that the deuterium at this position was exclusively transferred to the β-position of the carbonyl group (Scheme 2). Additionally, when the substrate possessing deuterium at the ortho- and para-positions of the phenyl ring (**1a**-d_3) was employed, deuterium was incorporated in the position α to the carbonyl.[11] Furthermore, when a

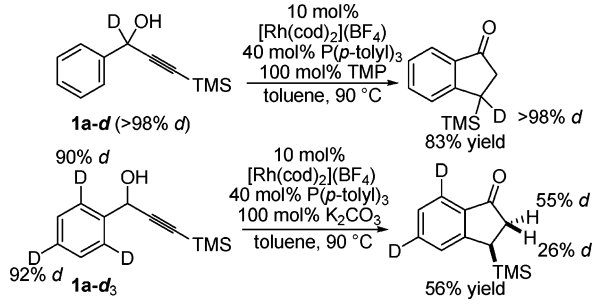
10.1021/ja042581o CCC: $30.25

Table 2. Catalytic Cyclization of Aryl- or Heteroaryl-prop-2-yn-1-ols[a]

Entry	Starting Material	Product
1	**1b** (R^1= OMe, R^2=TMS)	**2b** 72%[a]
2	**1c** (R^1= F, R^2=TMS)	**2c** 86%[b]
3	**1d** (R^1= H, R^2=Ph)	**2d** 39%[b]
4	**1e**	**2e** 43%[b]; **3e** 44%[b]
5	**1f**	**2f** 68%[c]; **3f** 18%[c]
6	**1g**	**2g** 51%[c]
7	**1h** (X= NTs)	**2h** 49%[a]
8	**1i** (X= S)	**2i** 31%[c,d]; **4i** 32%[c,d]
9	**1j** (X= S)	**4j** 95%[a]
10	**1k** (X= O)	**4k** 57%[a]

[a] Conditions: 10 mol % $[Rh(cod)_2](BF_4)$, 40 mol % P(*p*-tolyl)$_3$, 100 mol % TMP, toluene, 90 °C. [b] Reaction in THF at 67 °C. [c] Reaction in toluene at 100 °C. [d] 20 mol % of $[Rh(cod)_2](BF_4)$ and 80 mol % of P(*p*-tolyl)$_3$ were used.

Scheme 2

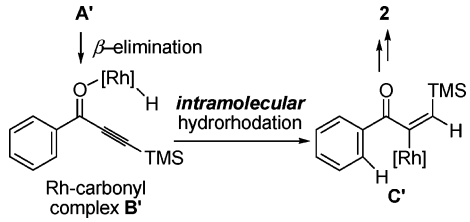


1:1 mixture of deuterium-labeled **1a** (**1a**-*d*) and unlabeled **1c** was treated with a catalytic amount of $[Rh(cod)_2](BF_4)$ and P(*p*-tolyl)$_3$ at room temperature, no deuterium was incorporated to **2c**.

These results indicated that the reaction proceeded as designed in the beginning (Scheme 1), and importantly, hydrorhodation of the alkynyl ketone intermediate **B′** occurred without dissociation of the Rh−hydride complex to produce alkenyl rhodium complex **C′** directly (Scheme 3).

In summary, we have developed a concise method for the construction of a cyclopentanone ring based on hydrorhodation-

Scheme 3



1,4-rhodium migration sequence. This method allows a very easy preparation of various types of cyclopentanone derivatives fused with aromatic ring from the corresponding aryl and heteroaromatic aldehydes.

Acknowledgment. This research was partly supported by the Novartis Science Foundation and a Grant-in-Aid for Scientific Research from Ministry of Education, Culture, Sports, Science and Technology of Japan. H.Y. was granted a Research Fellowship of the Japan Society for the Promotion of Science for Young Scientists.

Supporting Information Available: Preparative methods and spectral and analytical data of compounds **1**−**4** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) When $RuCl_2(PPh_3)_2$ or $[Ir(cod)_2](BF_4)$ + P(*p*-tolyl)$_3$ or $PtCl_2(cod)_2$ + P(*p*-tolyl)$_3$ was used instead of $[Rh(cod)_2](BF_4)$ + P(*p*-toyl)$_3$, oxidation of alcoholic substrate **1** was observed.
(10) The TMS group of the cyclized products **2i**−**2k** were readily desilylated under the reaction conditions.
(11) When TMP was employed as a base, a substantial amount of proton was incorporated to the α-position of the carbonyl. We believe that the proton comes from N−*H* of TMP via enolization under basic conditions.

JA042581O