Rhenium-catalyzed synthesis of indene derivatives via C–H bond activation*

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Abstract: Rhenium complex, $[ReBr(CO)_3(thf)]_2$-catalyzed reactions between aromatic imines and either acetylenes or α,β-unsaturated carbonyl compounds gave indene derivatives in good to excellent yields. These reactions proceed via C–H bond activation, insertion of acetylenes or α,β-unsaturated carbonyl compounds, intramolecular nucleophilic cyclization, and reductive elimination. Indene derivatives were also obtained from aromatic ketones and α,β-unsaturated carbonyl compounds in the presence of catalytic amounts of the rhenium complex and *p*-anisidine. Sequential ruthenium-catalyzed hydroamination of aromatic acetylenes with anilines, and rhenium-catalyzed reactions of the formed aromatic ketimines with α,β-unsaturated carbonyl compounds also provided indene derivatives.

*Keywords*: rhenium; C–H activation; indene; atom-economical.

INTRODUCTION

Cyclic compounds play an important role in generation of organic molecules. Thus, there has been a great deal of research on the syntheses, structures, reactivities, and functions of cyclic compounds. Indene frameworks are cyclic compounds that are frequently observed in bioactive species [1], functional materials [2], and ligands for metal complexes [3]. To date, various methods to synthesize indene derivatives have been reported [4]. However, transformations via C–H bond activation offer an efficient and atom-economical alternative, and can be considered as a useful new approach to indene frameworks.

Transition-metal-catalyzed transformations via C–H bond activation and successive insertion of unsaturated molecules are an important and challenging theme because carbon–carbon bond formation can be achieved in short reaction steps without the formation of byproducts such as metal halides. The first breakthrough came in 1993. Murai, Chatani, and Kakiuchi reported that a coupling reaction between acetophenone and a vinylsilane occurred with a catalytic amount of a ruthenium complex, $RuH_2(CO)(PPh_3)_3$ (eq. 1) [5]. After this report, many reactions initiated by C–H bond activation appeared [6]. These reactions proceeded by C–H bond activation with a ruthenium complex followed by insertion of a carbon–carbon double bond, and formal reductive elimination. Because the insertion occurred between the Ru–H bond, the reactions gave only a simple insertion product.
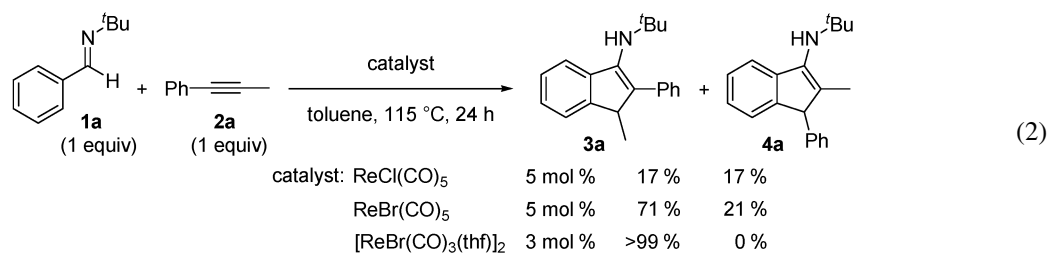
(1)
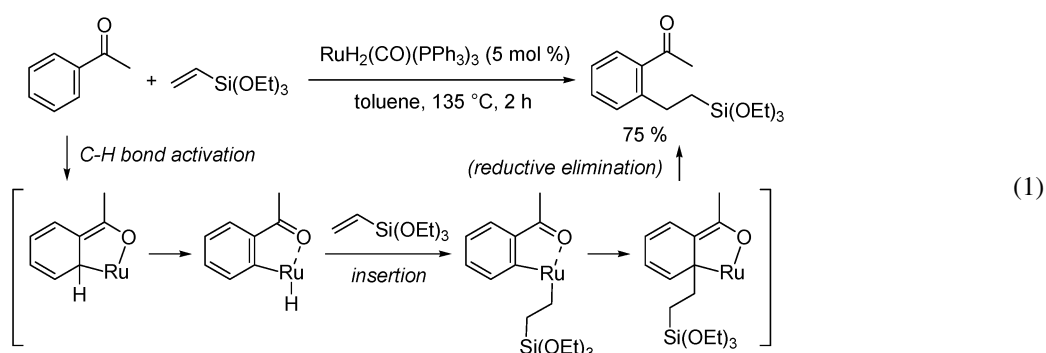
In order to obtain cyclic compound **C** from an aryl ketone and acetylene using C–H activation, the acetylene must be inserted into the M–C bond of **A**, not the M–H bond (Scheme 1). In addition, the nucleophilic cyclization from **B** should occur smoothly after the insertion step, otherwise reductive elimination from **B** gives insertion product **E**. So, we looked for a different metal which could hopefully facilitate the insertion into the M–C bond of **A**, and generate a polar M–C bond for intramolecular nucleophilic cyclization. From the value of electronegativity, we chose rhenium as the key atom.
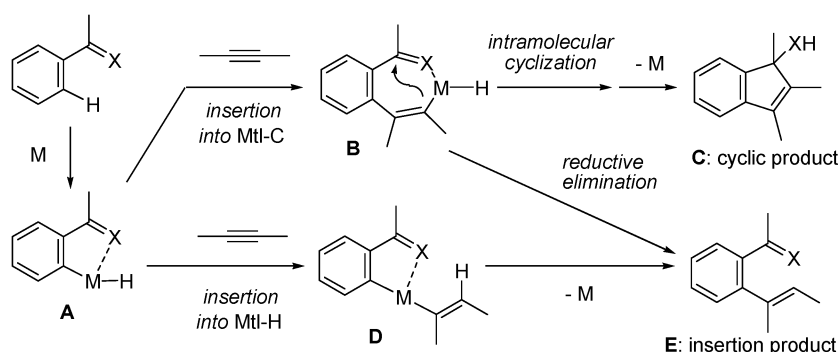
Scheme 1 Successive reactions after C–H bond activation.

SYNTHESIS OF INDENES FROM AROMATIC ALDIMINES AND ACETYLENES

At first, we examined the formation of indene derivatives by a reaction of acetophenone or dimethyl-hydrazone of benzaldehyde with 1-phenyl-1-propyne (**2a**) in toluene in the presence of a catalytic amount of $ReCl(CO)_5$ at reflux for 24 h. However, the reactions did not occur and all the reactants remained unchanged in both cases. Among the substrates examined, an imine of benzaldehyde, **1a**, was found to react with acetylene **2a** and gave two desired isomeric indene derivatives, **3a** and **4a**, directly in one operation [7a,b], though the yields were low (eq. 2). This result suggests that the imine nitrogen atom can coordinate more strongly to the rhenium center than the oxygen atoms, and that the rhenium complex can undergo C–H bond activation. In addition, a carbon–carbon triple bond was inserted into the Re–C bond and further intramolecular cyclization took place. This result is in sharp contrast to the reaction with $RuH_2(CO)(PPh_3)_3$ (eq. 1) [8].

$$
\textbf{1a} \; (1 \text{ equiv}) + \textbf{2a} \; (1 \text{ equiv}) \xrightarrow[\text{toluene, 115 °C, 24 h}]{\text{catalyst}} \textbf{3a} + \textbf{4a} \tag{2}
$$

catalyst: ReCl(CO)$_5$	5 mol %	17 %	17 %
ReBr(CO)$_5$	5 mol %	71 %	21 %
[ReBr(CO)$_3$(thf)]$_2$	3 mol %	>99 %	0 %

The yields and selectivity were improved by changing the ligand of the rhenium complex from chloride to bromide, and changing the two carbon monoxides to THFs. The indene derivative **3a** was obtained quantitatively with a rhenium complex, [ReBr(CO)$_3$(thf)]$_2$, under the same reaction conditions.

Treatment of aromatic aldimine **1a** with diphenylacetylene (**2b**) in the presence of the rhenium catalyst gave indene derivative **3b** in 96 % yield (Table 1, entry 1). Aldimines with electron-donating groups, such as methoxy and methyl groups at the *para*-position of the aldimine, gave the corresponding indene derivatives in excellent yields (Table 1, entries 2 and 3). However, an aldimine bearing an electron-withdrawing trifluoromethyl group at the *para*-position gave **3e** in low yield (Table 1, entry 4). The indene derivative was obtained in 40 % yield by the reaction of an aldimine bearing an *ortho*-methyl group with **2b** (Table 1, entry 5). From our experiments, it was found that acetylenes bearing at least one aryl group gave the corresponding indene derivatives (Table 1, entries 6 and 7).

Table 1 Rhenium-catalyzed reaction of an aromatic aldimine with an acetylene.

$$
\textbf{1} + \text{Ph}\!-\!\!\equiv\!\!-\text{R}^2 \; (\textbf{2}) \xrightarrow[\text{toluene, reflux, 24 h}]{[\text{ReBr(CO)}_3(\text{thf})]_2 \; (3.0 \text{ mol \%})} \textbf{3} + \textbf{4}
$$

| entry	imine (R^1)	acetylene (R^2)	% yield[a]	3:4[b]
1	H (**1a**)	Ph (**2b**)	**3b** 96 (>99)	
2	*p*-MeO (**1b**)	**2b**	**3c** 89 (96)	
3	*p*-Me (**1c**)	**2b**	**3d** 95 (>99)	
4	*p*-CF$_3$ (**1d**)	**2b**	**3e** 14 (16)	
5	*o*-Me (**1e**)	**2b**	**3f** 40 (52)	
6[c]	**1a**	^{n}C$_6$H$_{13}$ (**2c**)	**3g** 64 (68)	>99:<1
7	**1a**	SiMe$_3$ (**2d**)	**4h** 81 (87)	<1:>99

[a] Isolated yield. The yield determined by ^{1}H NMR is reported in parenthesis. [b] The ratios of indene derivatives **3** and **4**. [c] 135 °C.

SYNTHESIS OF INDENES FROM AROMATIC KETONES AND ACRYLATES

Next, we examined the reaction between ketimine **5a** and ethyl acrylate (**6**) with a catalytic amount of the rhenium complex. The expected nitrogen-substituted indane derivative **7a** was obtained in 64 % yield along with indene derivative **8a** in 11 % yield (eq. 3). The yield of **8a** derived by elimination of an amine after cyclization was increased by changing the substituent on the nitrogen of **5** from benzyl to phenyl and using a higher reaction temperature. Treatment of an aromatic ketimine **5b** with **6** in the presence of a catalytic amount of [ReBr(CO)$_3$(thf)]$_2$ in toluene at 180 °C gave indene derivative **8a** in 93 % yield (eq. 3) [7c]. The formation of indene derivative **8a** with the rhenium catalyst is in sharp contrast to the result with a Wilkinson catalyst, RhCl(PPh$_3$)$_3$, which catalyzes only C–H bond activation and insertion of an acrylate [9].

$$(3)$$

a: R = PhCH$_2$ 150 °C, 8 h   **7a**: 64 %   **8a**: 11 %
b: R = Ph   180 °C, 24 h   **7b**: 0 %   93 %
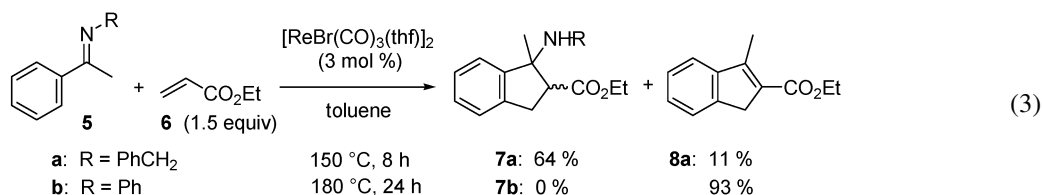
The proposed mechanism for the formation of indene derivatives **L** from ketimines **G** and acrylic esters is shown in Scheme 2. C–H bond activation of **G** is accelerated by the coordination of the nitrogen atom to a rhenium center. After C–H bond activation, the acrylate inserts into the Re–C bond of **H**. The intramolecular nucleophilic cyclization of the generated organorhenium species **I** to the imine group followed by reductive elimination gives **K**. Elimination of aniline from **K** affords the indene derivative **L**.
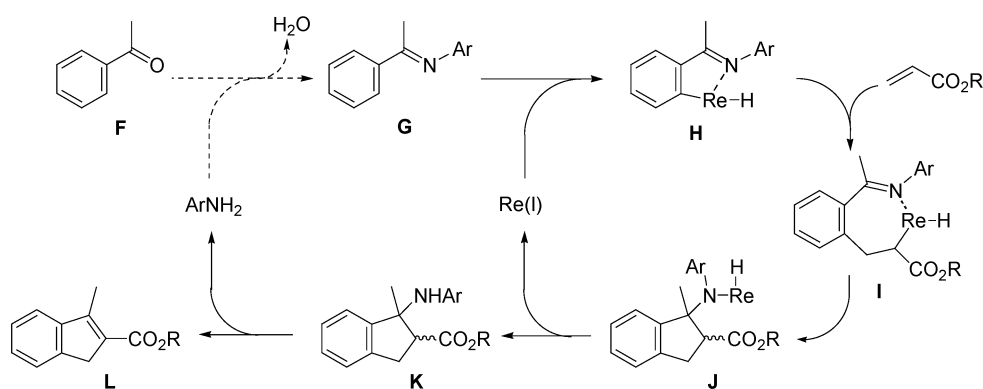
Scheme 2 Proposed mechanism for the synthesis of indenes.

In the reaction, aniline is formed as a side product. This result tells us that the reaction can be achieved by starting from aromatic ketones with a catalytic amount of aniline (drawn in broken arrows) if the imine formation is compatible with the rest of the reaction steps. Total transformation can be regarded as a formal [3+2] cycloaddition of aromatic ketones and acrylates by dehydration. The desired reaction proceeded with a catalytic amount of the rhenium complex and aniline (concentration of the reaction mixture: 0.5 M, 7 %). The yield was improved using *p*-anisidine in place of aniline, and by using a relatively high concentration (2.5 M) and temperature (Table 2, entry 1).

Aromatic ketones bearing a long alkyl chain or phenyl group, **9b** and **9c**, provided indene derivatives **8b** and **8c** in 84 and 72 % yields, respectively (Table 2, entries 2 and 3). Acetophenones bearing an electron-donating group at the *para*-position (**9d** and **9e**), afforded the corresponding indene derivatives **8d** and **8e** in good yields, respectively (Table 2, entries 4 and 5). On the other hand, the yield decreased using an acetophenone derivative bearing an electron-withdrawing group, **9f** (Table 2, entry 6). In the case of *o*-methylacetophenone (**9g**), the yield dropped to 11 % probably due to a steric factor (Table 2, entry 7). In the case of dissymmetric aryl ketones, **9h** and **9i**, a mixture of two indene derivatives was obtained in a ratio of 3:1 to 4:1 (Table 2, entries 8 and 9).

Table 2. Rhenium and aniline-catalyzed synthesis of indene derivatives from aromatic ketones and ethyl acrylate.[a]


entry	ketone	product	yield[b] / %
1	**9a** (R^1 = H, R^2 = Me)	**8a** (R^1 = H, R^2 = Me)	93 (99)
2[c]	**9b** (R^1 = H, R^2 =$^nC_5H_{11}$)	**8b** (R^1 = H, R^2 =$^nC_5H_{11}$)	84 (86)
3	**9c** (R^1 = H, R^2 = Ph)	**8c** (R^1 = H, R^2 = Ph,)	72 (74)
4	**9d** (R^1 = p-OMe, R^2 = Me)	**8d** (R^1 = p-OMe, R^2 = Me)	80 (82)
5	**9e** (R^1 = p-Me, R^2 = Me)	**8e** (R^1 = p-Me, R^2 = Me)	85 (89)
6	**9f** (R^1 = p-CF$_3$, R^2 = Me)	**8f** (R^1 = p-CF$_3$, R^2 = Me)	37 (53)
7	**9g** (R^1 = o-Me, R^2 = Me)	**8g** (R^1 = o-Me, R^2 = Me)	11 (16)

8   **9h** → **8ha** + **8hb**
68 (69) (**8ha** : **8hb** = 77 : 23)

9   **9i** → **8ia** + **8ib**
90 (93) (**8ia** : **8ib** = 80 : 20)

[a] Olefin (1.5 equiv). [b] Isolated yields. The yields determined by ^{1}H NMR are reported in parentheses. [c] 48 h.

SYNTHESIS FROM TERMINAL ACETYLES AND ACRYLATES

Another approach to prepare aromatic ketimines is hydroamination of aromatic acetylenes with amines. Thus, we examined the successive hydroamination of aromatic acetylenes and rhenium-catalyzed C–H bond activation of the formed aromatic ketimines leading to indenes [7d].

Treatment of phenylacetylene (**10**) with aniline in the presence of catalytic amounts of $Ru_3(CO)_{12}$ and NH_4PF_6 at 100 °C in toluene generated an aromatic ketimine, **5b** [10], which was then treated with ethyl acrylate (**6**) in the presence of $[ReBr(CO)_3(thf)]_2$, in toluene at 180 °C for 24 h. As a result, indene derivative **8a** was obtained in 82 % yield (eq. 4). A rhenium complex, $Re_2(CO)_{10}$, could also be used instead of $[ReBr(CO)_3(thf)]_2$.

(4)
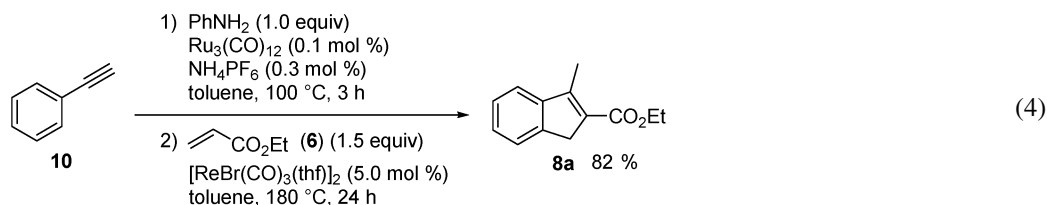
Because phenylacetylenes polymerize gradually with the rhenium complex, the yield of **8a** decreased to 21 % when both ruthenium and rhenium catalysts were added with aniline at the same time and the mixture was heated at 180 °C.

CONCLUSIONS

We have succeeded in rhenium-catalyzed synthesis of indene derivatives via C–H bond activation by the reactions of aromatic aldimines with phenyl acetylenes. Indenes were also synthesized by reactions between aromatic ketimines, aromatic ketones, or terminal aromatic acetylenes and acrylates. These reactions proceeded via C–H bond activation, insertion of unsaturated molecules, intramolecular nucleophilic cyclization, and reductive elimination. We hope that these reactions will become useful methods to synthesize indene frameworks.

ACKNOWLEDGMENTS

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