Chelation-Assisted Rh^I-Catalyzed *ortho*-Alkylation of Aromatic Ketimines or Ketones with Olefins

Chul-Ho Jun,* Choong Woon Moon, Jun-Bae Hong, Sung-Gon Lim, Kwan-Yong Chung, and Yeon-Hee Kim[a]

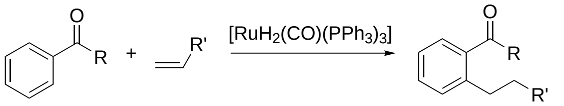
Abstract: Described herein is the Rh^I-catalyzed *ortho*-alkylation of aromatic ketimines or ketones with olefins. This method showed high reactivity and selectivity to monoalkylation for a variety of olefins including 1-alkenes with an allylic proton, α,ω-dienes, and internal olefins. For a mechanistic study, H/D exchange experiments were carried out, which demonstrated that the *ortho* C–H bond could be easily cleaved even at the low temperature of 45 °C. The key step of this reaction is the formation of a stable five-membered metallacycle by a chelation-assisted *ortho* C–H bond activation. Furthermore, the direct *ortho*-alkylation of aromatic ketones with the Rh^I complex was successfully achieved by adding 50 mol% of benzylamine as a chelation-assistant tool.

Keywords: alkenes · alkylation · C–H activation · metalation · Wilkinson's catalyst

Introduction

Transition metal catalyzed C–H bond activation is one of the attractive areas of modern organic chemistry.[1] The direct functionalization of unreactive C–H bonds can lead to a new synthetic route for constructing organic molecules. This process has the benefits of great selectivity and involves relatively few atoms.[2] Moreover, it is an environmentally friendly process compared with the conventional methods such as carbon–halide functionalization.[3]

In 1993, Murai and co-workers reported the first example of a highly efficient and synthetically useful C–H bond activation, which is an *ortho*-alkylation[4] of aromatic ketones and imines with olefins in the presence of a ruthenium catalyst [Eq. (1)].[5] In general, electrophilic alkyl substitution of the aromatic ring with an electron-donating substituent gives a mixture of *ortho*- and *para*-isomers, where the latter is a major product.[6] The electron-deficient aromatic rings such as acylbenzene derivatives are known to be poor substrates for an alkylation. However, Murai's reaction gave rise to the selective *ortho*-alkylation of acylbenzene derivatives. It should be noted that this *ortho*-alkylation affords a new type of aromatic compounds, which cannot be easily obtained by the conventional synthetic methods.



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The application of Murai's *ortho*-alkylation to the synthesis of natural products was demonstrated by Woodgate's group.[7] For the functionalization of the ring C aromatic diterpenoids, the *ortho*-alkylation of 1-(hydroxyphenyl)ethanone equivalents was carried out with $[Ru(CO)_2(PPh_3)_3]$. Weber and co-workers reported the copolymerization of acetophenone having two free *ortho* C–H bonds and α,ω-dienes bearing vinylsilane functionalities in the presence of $[RuH_2(CO)(PPh_3)_3]$.[8]

In spite of the excellence of Murai's reaction in terms of efficiency, there is a limitation in terms of the selection of an olefin as an alkylating partner.[5b, c] While vinylsilane derivatives were very effective olefins, several types of olefins such as dienes, internal olefins, and olefins having electron-withdrawing or electron-donating groups showed a low reactivity toward an *ortho*-alkylation. In addition, 1-alkenes bearing primary or secondary alkyl substituents turned out to be inapplicable, probably due to facile olefin isomerization.

Recently, Brookhart and Lenges reported that the rhodium bis-olefin complex $[C_5Me_5Rh(C_2H_3SiMe_3)_2]$ was shown to be a catalyst for the selective addition of olefins to the *ortho* position of aromatic ketones.[9] According to H/D exchange experiments, this rhodium complex activated all sites (*ortho*, *meta*, *para*) of the substrate, while Murai's Ru-catalyzed process only caused the activation of the *ortho* C–H bonds.

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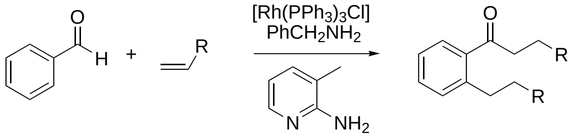
More recently, in the course of the investigation of the efficient catalytic hydroacylation,[10] we found the domino reaction of hydroacylation and *ortho*-alkylation with the cocatalyst system of Wilkinson's complex and benzylamine [Eq. (2)].[11]



(2)

After further investigation of this reaction sequence, we found that the initial chelation-assisted hydroacylation took place to give the corresponding ketimine, which then underwent *ortho*-alkylation with the remaining olefins. With the aromatic ketimines as the starting substrate, therefore, the aromatic C–H/olefin coupling reaction with the rhodium catalyst was successfully developed. In this paper, we discuss in detail the scope and the mechanism of the Rh-catalyzed *ortho*-alkylation of aromatic ketimines as well as ketones.

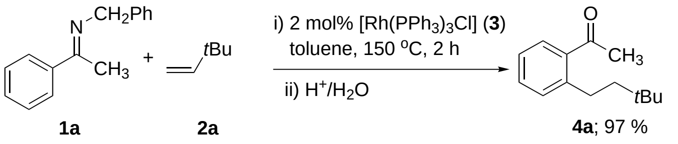
Results and Discussion

1. The scope of *ortho*-alkylation of aromatic ketimines: In a previous study, we discovered that Rh^I-catalyzed *ortho*-alkylation with olefin occurred for ketimine. When the benzylimine of acetophenone (**1a**) was treated with olefin **2a** in toluene at 150 °C for 2 h in the presence of $[Rh(PPh_3)_3Cl]$ (**3**, 2 mol%), *ortho*-alkylation of **1a** took place to produce **4a** in a 97% isolated yield after hydrolysis [Eq. (3)]. In the case of acetophenone (**5a**), however, no *ortho*-alkylation product was obtained under the same reaction conditions [Eq. (4)].

Abstract in Korean:

본 논문은 로듐 (I) 촉매 하에서 올레핀과 방향족 케티민 및 케톤의 오르토-알킬화 반응에 관하여 기술하고 있다. 이 반응은 알릴릭 수소를 가진 1-알켄과, α,ω-다이엔 그리고 인터널 올레핀 등을 포함하는 다양한 올레핀에 대해서 높은 반응성과 모노 알킬화 반응을 하는 선택성을 보여주었다. 메커니즘 연구를 위한 수소/이중수소 (H/D) 교환 실험을 통해서, 오르토 탄소-수소 결합이 45 ℃ 정도의 낮은 온도에서도 쉽게 끊어질 수 있다는 것을 확인하였다. 이 반응의 가장 중요한 단계는 킬레이션에 의한 오르토 탄소-수소 결합 활성을 통해서 안정한 오각형의 금속고리 화합물을 형성하는 것이다. 그리고 킬레이션 보조제로서 작용할 수 있는 벤질아민 (50 mol%)을 첨가함으로써, 로듐 (I) 촉매 하에서 방향족 케톤의 오르토-알킬화 반응을 성공적으로 수행할 수 있었다.

In an analogous way to Murai's *ortho*-alkylation via a five-membered metallacycle **6**, this Rh^I-catalyzed *ortho*-alkylation is believed to occur by the formation of the stable metallacycle **7**, which results from the chelation-assisted C–H bond activation (Scheme 1). This Rh^I-catalyzed reaction utilizes the precoordination of Rh^I to the nitrogen of the imine in contrast to the chelation of the carbonyl to Ru^{II} in Murai's reaction. As a result, it implies that the rhodium complex could not coordinate effectively to the oxygen of the carbonyl group to cleave the aromatic sp^2 C–H bond and generate metallacycle **8**, while the ruthenium might be oxophilic enough to coordinate it.



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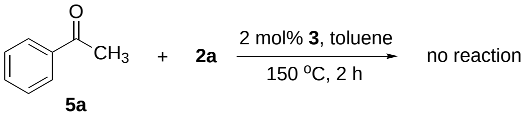

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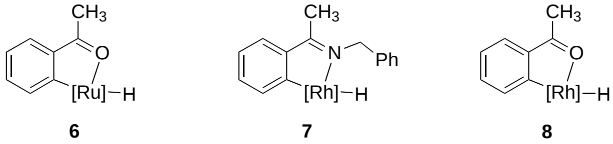

Scheme 1. Five-membered metallacycles by the chelation-assisted C–H bond activation.

Optimization of Rh^I-catalyzed ortho-alkylation: A variety of transition metal complexes were tested for the *ortho*-alkylation of an aromatic ketimine. Most metal complexes such as $[Rh(CO)(PPh_3)_2Cl]$, $[Rh(CO)(PPh_3)_3H]$, $[\{RhCl(C_8H_{14})_2\}_2]$, $[Ir(CO)(PPh_3)_2Cl]$, $[Ru_3(CO)_{12}]$, $[RuH_2(CO)(PPh_3)_3]$, and $PdCl_2/Ph_3P$ did not show any activity for *ortho*-alkylation. Only Rh complexes generated in situ from the addition of a phosphane ligand to $[\{RhCl(C_8H_{14})_2\}_2]$ were able to undergo *ortho*-alkylation. The Rh complexes displayed different activities depending on the added phosphane ligand (Table 1).

The electron-rich phosphane ligand bearing an electron-donating substituent showed high reactivity (entries 1–3). The sterically more demanding $P(o\text{-tolyl})Ph_2$ gave a lower yield of **9** (entry 4). With aliphatic phosphane ligands, no *ortho*-alkylation occurred (entries 5 and 6). The bidentate ligands led to very low yields of *ortho*-alkylated products (entries 7 and 8), but DPPP (1,3-bis(diphenylphosphino)propane) having a big bite angle showed good reactivity probably due to acting as a monodentate ligand (entry 9).[12]

In order to optimize the reaction conditions, we performed the reaction of **1a** and **2a** with 2 mol% of **3** at various reaction temperatures (Figure 1). The reaction was monitored by checking the yield of the *ortho*-alkylated product, and it was improved as the reaction temperature was raised to 150 °C. At

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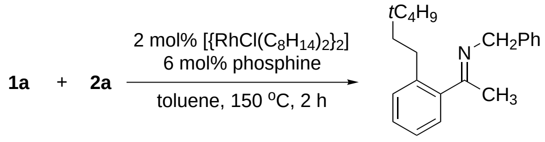
Table 1. The effect of the phosphane ligand in *ortho*-alkylation.



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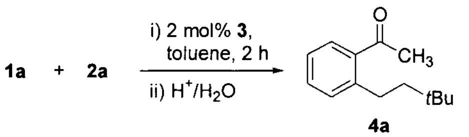
	phosphane ligand	yield [GC, %]
1	PPh_3	92
2	$P(4\text{-}MeOC_6H_4)_3$	96
3	$P(4\text{-}MeC_6H_4)_3$	87
4	P(*o*-tolyl)Ph_2	61
5	PCy_3	0
6	PMe_3	0
7	DPPM[a]	28
8	DPPE[a]	8
9	DPPP	77

[a] DPPM (bis(diphenylphosphino)methane). DPPE (1,2-bis(diphenylphosphino)ethane).

180 °C, however, the yield of the product decreased. Thus, the best result was obtained at 150 °C in approximately 2 h in the presence of 2 mol% of **3**.



4a

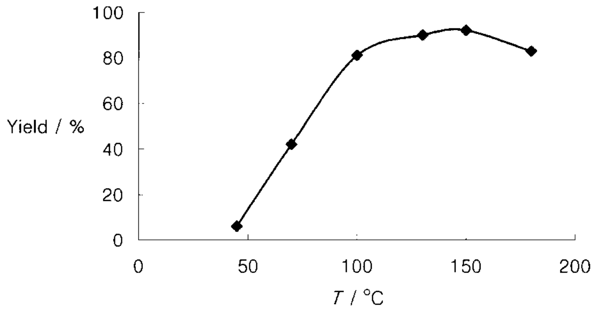
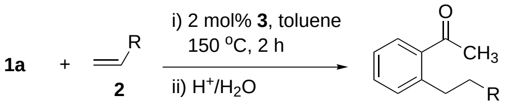


Figure 1. The effect of temperature on the reaction of **1a** and **2a** with 2 mol% of **3**.

ortho-Alkylation with various olefins: Ketimine **1a**, generated by the condensation of acetophenone and benzylamine, reacted with various 1-alkenes **2** in the presence of 2 mol% of **3** at 150 °C for 2 h to give, after hydrolysis, the corresponding *ortho*-alkylated ketones (Table 2).

In Murai's Ru^{II}-catalyzed *ortho*-alkylation, 1-alkenes bearing an allylic proton gave low yields due to a facile olefin isomerization.[5b] However, our Rh-catalyzed reaction afforded high efficiency for *ortho*-alkylation even with 1-alkenes having an allylic proton (entries 1–5). Vinyltrimethylsilane (**2h**), an olefin substrate used for the Murai's *ortho*-alkylation, was also an effective substrate (entry 8). In general, most alkyl and aryl olefins showed good to moderate reactivities. However, heteroatom-containing olefins such as allyl ether (**2j**) and allyl amine (**2l**) turned out to be poor substrates for this *ortho*-alkylation (entries 9–12). In the case of α,ω-diene (**2m**), the addition of an aromatic C–H bond took place at the one end, and the other end of the olefin was isomerized into the internal olefin (internal:terminal = 95:5). Thus, the product was isolated as a single compound with a high yield (92%) after hydrogenation of the isomeric mixture (entry 13).

Table 2. Rh^I-catalyzed *ortho*-alkylation of ketimine with 1-alkenes.



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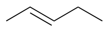
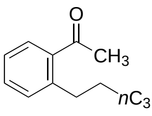
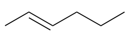
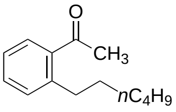
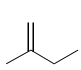
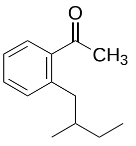
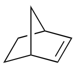
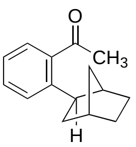
	2; R	isolated yield of **4** [%][a]
1	**2a**; *t*Bu	**4a**, 97%
2	**2b**; *n*Bu	**4b**, 94%[b]
3	**2c**; *n*C_6H_{13}	**4c**, 71%[b]
4	**2d**; *n*$C_{10}H_{21}$	**4d**, 82%[b]
5	**2e**; Cy	**4e**, 65%
6	**2f**; C_6F_5	**4f**, 91%
7	**2g**; Ph	**4g**, 41%
8	**2h**; $SiMe_3$	**4h**, 92%
9	**2i**; CH_2OH	**4i**, 0%
10	**2j**; CH_2OEt	**4j**, (4%)
11	**2k**; CH_2OAc	**4k**, 0%
12	**2l**; CH_2NMe_2	**4l**, 0%
13	**2m**; $(CH_2)_6CH{=}CH_2$	**4m**, 92%[c]

[a] GC yields are given in parenthesis. [b] Reaction time: 6 h. [c] Isolated yield after hydrogenation (Pd/C and H_2) of the isomeric mixture with internal and terminal olefins (95:5).

Internal olefins were also applied for the reaction with **1a** under the same reaction conditions (Table 3). In the cases of

Table 3. Rh^I-catalyzed *ortho*-alkylation of ketimine with internal alkenes.

$$\mathbf{1a} + \mathbf{2} \xrightarrow[\text{ii) H}^+/\text{H}_2\text{O}]{\text{i) 2 mol\% }\mathbf{3}\text{, toluene, 150 °C, 2 h}} \mathbf{4}$$

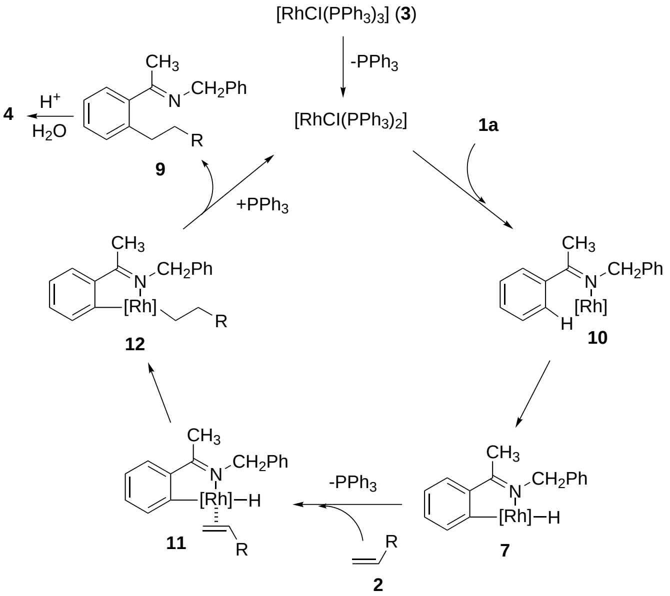
	2	**4**	isolated yield [%]
1	 **2n**	 **4n**	95
2	 **2o**	 **4b**	42[a]
3	 **2p**	 **4p**	35[a]
4	 **2q**	 **4q**	92

[a] Reaction time: 6 h.

2-pentene (**2n**) and 2-hexene (**2o**), the linear alkylation products (**4n** and **4b**) were unexpectedly obtained, probably due to the facile isomerization of the internal olefin to the terminal olefin (entries 1 and 2). Even sterically hindered dialkyl-substituted olefin **2p** underwent the *ortho*-alkylation with a moderate reactivity (entry 3). Although cycloalkenes such as cyclohexene and cyclopentene failed to cause the *ortho*-alkylation of **1a**; norbornylene (**2q**) gave a high yield (92%) of product **4q** with exclusive *exo*-selectivity (entry 4).

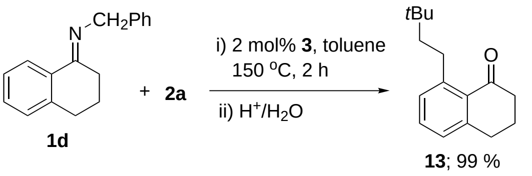
2. Mechanistic considerations for *ortho*-alkylation of aromatic ketimines

The mechanism of the Rh^I-catalyzed ortho-alkylation of aromatic ketimines: The proposed mechanism of *ortho*-alkylation is depicted in Scheme 2. At first, coordination of ketimine to the Rh^I complex (**3**) followed by the oxidative addition of an *ortho* C–H bond generates rhodium hydride **7**. Then, the hydrometalation of **7** into olefin **2** and the reductive elimination of the resulting intermediate **12** afford the *ortho*-alkylated ketimine **9**, which is easily hydrolyzed to give the final product **4**.



Scheme 2. The postulated mechanism of *ortho*-alkylation.

The formation of metallacycle **7** is the key step in this process. The significance of cyclometalation was demonstrated by the *ortho*-alkylation of the following cyclic ketimines. Ketimine **1d** derived from α-tetralone (**5b**) reacted with **2a** in the presence of 2 mol% of **3** to give the corresponding product **13** in a quantitative yield after hydrolysis [Eq. (5)]. However, the reaction of ketimine **1e** generated from 1-indenone produced no *ortho*-alkylated product under the same conditions [Eq. (6)].



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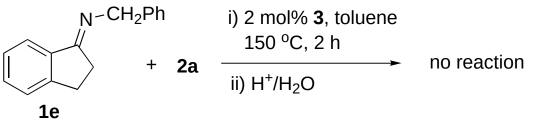
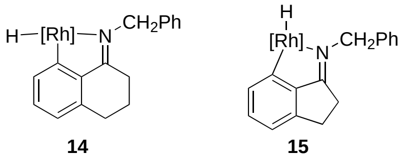


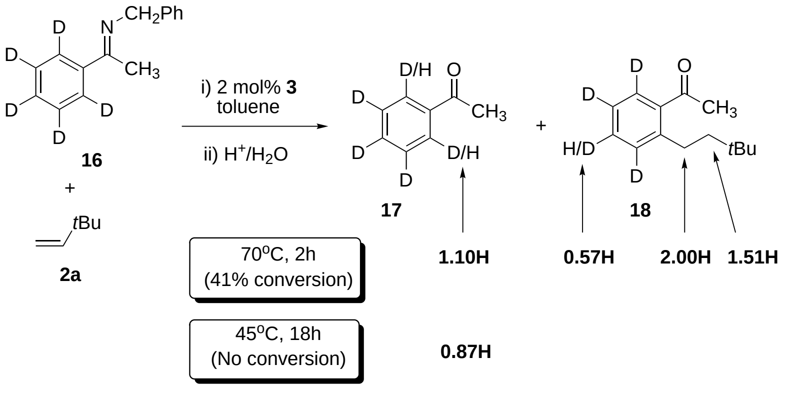
(6)

These results can be explained by the stability of the 5-membered metallacycle intermediates (Scheme 3). Whereas ketimine **1d** can readily form the stable metallacycle **14**, the formation of **15** from ketimine **1e** is not favored due to the angle strain. Therefore, the formation of a stable 5-membered metallacycle seems to be the most critical step.



Scheme 3. The stability of 5-membered metallacycles.

H/D exchange experiments: According to the previous reports by Murai[5b] and Brookhart,[9] the reaction steps of the *ortho*-alkylation, prior to reductive elimination, are in rapid equilibrium, and the rate-determining step is not an *ortho* C–H bond cleavage but the reductive elimination. Thus, we have also executed a H/D exchange experiment by using ^{1}H NMR spectroscopy to obtain such mechanistic information. It was carried out with the ketimine **16** derived from [D$_5$]acetophenone at 45 °C and 70 °C, respectively. The integration data for the products in ^{1}H NMR spectroscopy are shown in Equation (7). At 70 °C, the *ortho*-alkylation reaction took place to give a 41% yield of the alkylation product (**18**) with the H/D scrambled product (**17**) only at the *ortho* position. In the ^{1}H NMR spectrum of the product **18**, it is very interesting that a H/D exchange was observed at the



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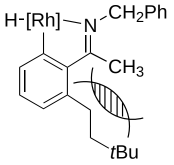
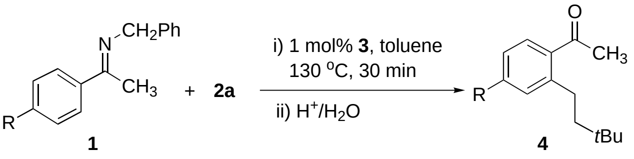


Scheme 4. The second *ortho* C–H bond cleavage obstructed by steric hindrance.

para position, not at the *ortho* position. This result might be explained by the fact that the *para* C–H bond could be cleaved, whereas the other *ortho* C–H bond was not activated probably due to the steric hindrance after the first *ortho*-alkylation occurred, as shown in Scheme 4. At the lower temperature (45 °C), no *ortho*-alkylation product was obtained even in 18 h, and the H/D scrambled product (**17**) only at the *ortho* position was observed. Therefore, this result is similar to Murai's, which means that the final step, reductive elimination, would be the rate-determining step in our reaction.

The effect of substituents at the aromatic ketimine: To investigate the substituent effect at the aromatic ring of ketimines, control experiments with *para*-substituted ketimines were carried out [Eq. (8)]. The ketimine having an electron-withdrawing group (–CF_3) at the *para* position showed a much better reactivity than the one with an electron-donating group (–OCH_3). Interestingly, this result is exactly the opposite of that from Murai's *ortho*-alkylation of aromatic ketones, which is accelerated by the electron-donating groups rather than the electron-withdrawing groups at the *para* position.[5d] This might be explained by the degree of coordination between the nitrogen or oxygen atom and the metal in this type of *ortho*-alkylation. For example, in the case of the methoxy group (–OCH_3), such coordination in our reaction is too strong for the whole catalytic process to occur.



(8)

R = CF_3 (**1b**) **4r**; 76
H (**1a**) **4a**; 56
CH_3O (**1c**) **4s**; 42

3. *ortho*-Alkylation of the aromatic ketones by utilizing a chelation-assistant tool: We were intrigued by establishing a method for the direct Rh^I-catalyzed *ortho*-alkylation of the aromatic ketones without the prior preparation for the corresponding ketimines. As mentioned earlier, the *ortho*-alkylation of the aromatic ketone was unsuccessful with the same catalyst system as that used for ketimines. Recently, we have reported amine-assisted hydroacylation, in which 2-amino-3-picoline or aniline was used as a chelation-assistant tool.[10d, e] In a similar manner, we adopted an alternative route by in situ generation of the corresponding ketimine from the aromatic ketone by adding an amine such as benzylamine.

Amines as a chelation-assistant tool: At first, the *ortho*-alkylation of acetophenone (**5a**) with **2a** in the presence of 5 mol % of **3** was examined by adding benzylamine in various concentrations (Figure 2).[13] As expected, addition of benzylamine gave rise to the *ortho*-alkylation of **5a**. The best result was obtained at 50 mol % of added benzylamine. Interestingly, the yield of product **4a** decreased gradually as benzylamine was added to more than 50 mol % based on **5a**.

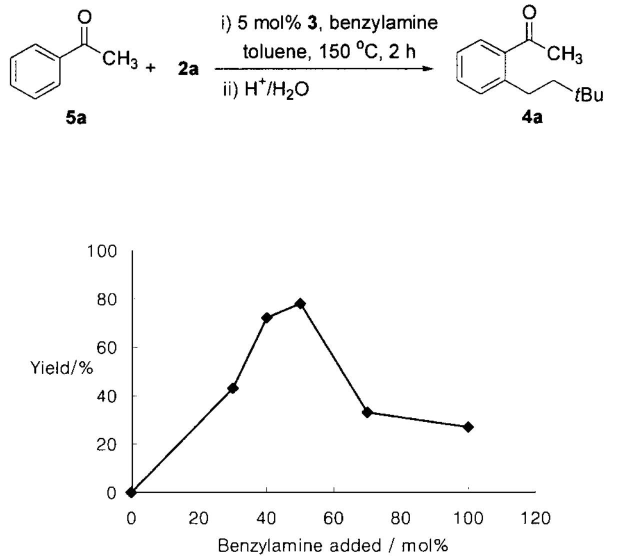
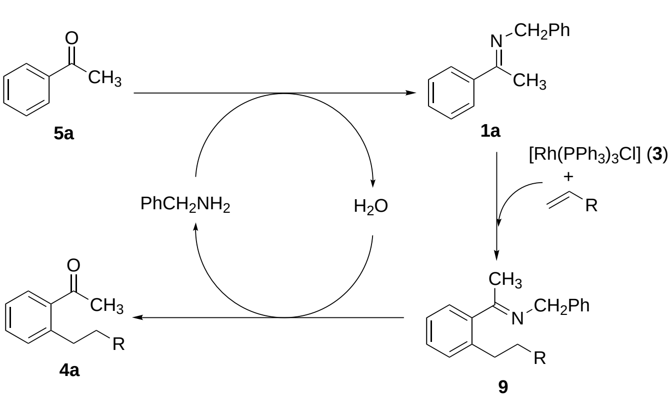


Figure 2. *ortho*-Alkylation of ketones catalyzed by Rh^I and benzylamine.

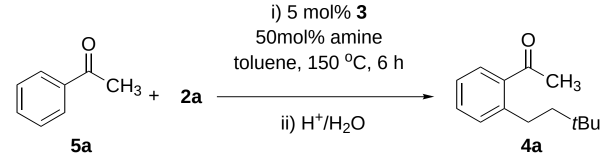
As a consequence of its high concentration, free benzylamine might replace phosphane ligands of complex **3**, which presumably makes the catalyst inactive. As a result, benzylamine seemed to serve as a chelation-assistant tool when it was employed as a cocatalyst for the reaction of aromatic ketones (Scheme 5).

In addition, several amines were tested instead of benzylamine to compare their reactivity as a chelation tool (Table 4). Most primary amines such as phenethylamine, aniline, and cyclohexylamine showed moderate activity (entries 2–4), whereas diethylamine showed no activity (entry 5). In entry 1, the use of benzylamine gave the highest yield (98 %) of the alkylated product. In fact, among the ketimines generated from acetophenone and various amines, the benzylamine-derived one showed the best reactivity and selectivity to



Scheme 5. *ortho*-Alkylation of aromatic ketones by utilizing a chelation-assistant tool.

Table 4. Amines as a chelation-assistant tool.

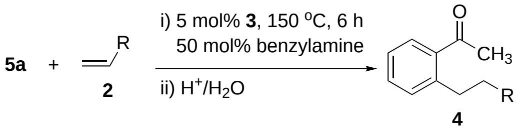


	amine	GC yield [%]
1	$PhCH_2NH_2$	98
2	$PhCH_2CH_2NH_2$	55
3	$PhNH_2$	53
4	$C_6H_{11}NH_2$	43
5	$(C_2H_5)_2NH$	trace

monoalkylation. Therefore, benzylamine turned out to be the best as a cocatalyst for the *ortho*-alkylation of aromatic ketones.

ortho-Alkylation of acetophenone (**5a**) *with various olefins*: With the cocatalyst system of **3** (5 mol%) and benzylamine (50 mol%), the *ortho*-alkylation of acetophenone (**5a**) was carried out with various olefins **2** (Table 5). Good reactivity was exhibited for most olefins except 1-dodecene (**2c**) containing a long alkyl chain (entries 3–4).

Table 5. *ortho*-Alkylation of acetophenone assisted by benzylamine.

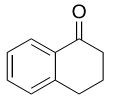
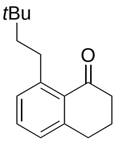
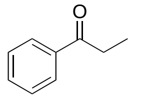
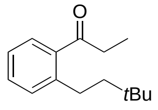
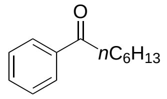
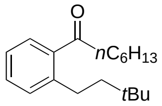
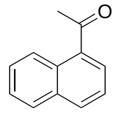
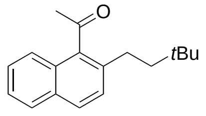
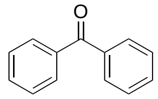
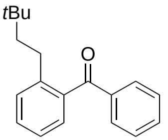


	2 (R)	isolated yield [product, %]
1	**2a** (*t*Bu)	**4a**, 95%
2	**2b** (*n*Bu)	**4b**, 72%
3	**2d** ($nC_{10}H_{21}$)	**4d**, 17%
4	**2e** (Cy)	**4e**, 89%
5	**2f** (C_6F_5)	**4f**, 68%

ortho-Alkylation of various aromatic ketones: Various aromatic ketones were, in turn, tested for *ortho*-alkylation with *tert*-butylethylene (**2a**) with the same cocatalyst system (Table 6). This method seems to be applicable to *ortho*-alkylation for most aromatic ketones (entries 1–3). However, the reactions of 1-acetonaphthone (**5e**) and benzophenone (**5f**) gave trace amounts of the desired *ortho*-alkylation products, which is presumably caused by difficulty with the condensation of ketone and benzylamine (entries 4–5).[14]

Table 6. *ortho*-Alkylation of aromatic ketones by utilizing benzylamine.

$$\text{ketone } (\mathbf{5}) + \mathbf{2a} \xrightarrow[\text{ii) H}^+/\text{H}_2\text{O}]{\text{i) 5 mol\% } \mathbf{3}\text{, 150 °C, 6 h; 50 mol\% benzylamine}} \text{product}$$

	ketone (**5**)	product	isolated yield [%]
1	 **5b**	 **13**	87
2	 **5c**	 **19c**	86
3	 **5d**	 **19d**	72
4	 **5e**	 **19e**	trace
5	 **5f**	 **19f**	trace

Conclusion

We have developed the Rh^I-catalyzed *ortho*-alkylation of aromatic ketimines with olefins. The key step of this reaction is the formation of a stable five-membered metallacycle by chelation-assisted *ortho* C–H bond activation. The advantages of this method are not only high efficiency for monoalkylation but also applicability to a variety of olefins including 1-alkenes with an allylic proton, α,ω-dienes, and internal olefins. Furthermore, the direct *ortho*-alkylation of aromatic ketones with the Rh^I complex was also achieved by adding 50 mol% of benzylamine as a chelation-assistant tool. H/D exchange experiments for mechanistic studies in this *ortho*-alkylation demonstrated the selectivity for the activation of *ortho* C–H bonds of aromatic ketimines. We are investigating the extension of this method to alkynes instead of olefins and the synthetic application for aromatic compounds.

Experimental Section

Materials: All the commercially available reagent-grade chemicals were purchased from Aldrich. Toluene was distilled over Na/benzophenone. $[RhCl(PPh_3)_3]$ was prepared according to the literature procedure.[15] Ketones used were commercially available, and all ketimines were synthesized from the corresponding ketone and an amine according to literature procedures.[16]

Typical procedure for *o*-alkylation of ketimine with olefin: A screw-capped pressure vial (1 mL) was charged with benzyl-(1-phenylethylidene)-amine (**1a**, 67.7 mg, 0.324 mmol), *tert*-butylethylene (**2a**, 32.7 mg, 0.389 mmol), $[RhCl(PPh_3)_3]$ (**3**, 6 mg, 0.00649 mmol, 2 mol% based upon **1a**), and toluene (0.1 g), and the mixture was stirred in an oil bath at 150 °C for 2 h. After the resulting ketimine was hydrolyzed by using a HCl solution (1N), the reaction mixture was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 5:2) to yield 64.1 mg (97%) of 1-[2-(3,3-dimethylbutyl)phenyl]-ethanone (**4a**).

Characterization data. 1-[2-(3,3-dimethylbutyl)phenyl]-ethanone (4a): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (dd, ^3J(H,H) = 8.8 Hz, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.8 (m, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.4 (t, ^3J(H,H) = 7.5 Hz, 2H; CH$_2$), 1.0 (s, 9H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (C=O), 144–125 (Cs in phenyl group), 46.6, 30.8, 30.4, 29.6, 29.4; MS: m/z (%): 204 (16) $[M]^+$, 189 (13), 148 (11), 147 (100), 133 (22), 131 (23), 129 (18), 119 (14); IR (neat): $\tilde{\nu} = 2954$, 2866, 1688 (CO), 1599, 1571, 1476, 1364, 1247, 950, 757 cm^{-1}; HRMS calcd for $C_{14}H_{20}O$ $[M]^+$ 204.151415; found: 204.151783.

1-(2-Hexyl-phenyl)-ethanone (4b): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (d, ^3J(H,H) = 9.3 Hz, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.9 (t, ^3J(H,H) = 7.6 Hz, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.5 (m, 2H; β-CH$_2$ in hexyl group), 1.4–1.2 (m, 6H), 1.0 (t, ^3J(H,H) = 6.5 Hz, 3H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (CO), 143–125 (Cs in phenyl group), 34, 32, 31.8, 30, 29.6, 22.8, 14.2; IR (neat): $\tilde{\nu} = 2927$, 2856, 1687 (CO), 1600, 1571, 1484, 1459, 1355, 1252, 954, 908, 759, 734, 598 cm^{-1}; MS: m/z (%): 204 (16) $[M]^+$, 189 (100), 147 (23), 143 (17), 133 (16), 131 (11), 119 (49), 117 (14), 91 (31).

1-(2-Dodecyl-phenyl)-ethanone (4d): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (dd, ^3J(H,H) = 7.5 Hz, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.9 (t, ^3J(H,H) = 7.6 Hz, 2H; α-CH$_2$ in dodecyl group), 2.6 (s, 3H; CH$_3$ to CO), 1.6 (m, 2H; β-CH$_2$ in dodecyl group), 1.3 (m, 18H), 0.9 (t, ^3J(H,H) = 6.2 Hz, 3H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (CO), 143–125 (Cs in phenyl group), 34, 32.1, 32, 30, 29.9, 29.8, 29.7, 29.6, 29.5, 22.8, 14.2; IR (neat): $\tilde{\nu} = 2925$, 2854, 1688 (CO), 1600, 1571, 1484, 1354, 1249, 954, 758, 597 cm^{-1}; MS: m/z (%): 288 (14) $[M]^+$, 274 (22), 273 (100), 147 (24), 143 (24), 134 (17), 129 (18), 119 (39), 117 (13), 91 (18), 43 (31); HRMS calcd for $C_{20}H_{32}O$ $[M]^+$ 288.245316; found: 288.245239.

1-[2-(2-Cyclohexyl-ethyl)-phenyl]-ethanone (4e): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (d, ^3J(H,H) = 7.4 Hz, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.9 (t, ^3J(H,H) = 7.9 Hz, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.8–1.6 (m, 5H), 1.5–1.4 (m, 2H), 1.3–1.1 (m, 4H), 1.0 (m, 2H); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202.5$ (CO), 143–125 (Cs in phenyl group), 39.9, 38.1, 33.4, 31.6, 30.1, 26.8, 26.5; IR (neat): $\tilde{\nu} = 2923$, 2850, 1687 (CO), 1600, 1571, 1484, 1445, 1354, 1250, 953, 758 cm^{-1}; MS: m/z (%): 230 (22) $[M]^+$, 215 (46), 147 (54), 143 (24), 134 (79), 133 (28), 129 (22), 119 (100), 91 (20), 43 (19); HRMS calcd for $C_{16}H_{22}O$ $[M]^+$ 230.167066; found: 230.167183.

1-[2-(2-Pentafluorophenyl-ethyl)phenyl]-ethanone (4f): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.8$ (dd, ^3J(H,H) = 8.8 Hz, 1H; Ar), 7.4 (m, 2H; Ar), 7.1 (dd, ^3J(H,H) = 7.8 Hz, 1H; Ar), 3.2 (m, 2H), 3.1 (m, 2H), 2.6 (s, 3H; CH$_3$ to CO); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (CO), 141–127 (Cs in phenyl group and pentafluorophenyl group), 30.1, 29.6, 24.2; IR (solid): $\tilde{\nu} = 3019$, 1684 (CO), 1519, 1503, 1357, 1252, 1216, 1120, 1024, 966, 946, 765, 669 cm^{-1}; MS: m/z (%): 314 (22) $[M]^+$, 299 (46), 134 (11), 133 (100), 105 (18), 103 (18), 90 (11), 79 (12), 77 (13), 43 (11); HRMS calcd for $C_{16}H_{11}F_5O$ $[M]^+$ 314.073006; found: 314.072807.

1-(2-Phenethyl-phenyl)-ethanone (4g): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.7$–7.1 (m, 9H; Ar), 3.2 (m, 2H), 2.9 (t, ^3J(H,H) = 7.6 Hz, 2H; CH$_2$), 2.6 (s, 3H; CH$_3$ to CO); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (CO), 143–125 (Cs in phenyl group), 38.1, 36.2, 29.5; IR (neat): $\tilde{\nu} = 1691$ cm^{-1} (CO); MS: m/z (%): 224 (6) $[M]^+$, 210 (13), 209 (76), 133 (52), 105 (15), 103 (16), 91 (100), 90 (10), 89 (10), 79 (11), 77 (16).

1-[2-(2-Trimethylsilanyl-ethyl)-phenyl]-ethanone (4h): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (dd, ^3J(H,H) = 7.6 Hz, 1H; Ar), 7.4 (m, 1H; Ar) 7.2 (m, 2H; Ar), 2.8 (m, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 0.8 (m, 2H), 0.1 (s, 9H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (C=O), 132–125 (Cs in phenyl group), 30.0, 28.4, 19.6, −1.7 (CH$_3$); IR (neat): $\tilde{\nu} = 2953$, 1687, 1599, 1570, 1446, 1355, 1246, 1175, 1095, 954, 910, 860, 841, 757 cm^{-1}; MS: m/z (%): 220 (8) $[M]^+$, 205 (100), 147 (17), 115 (18), 75 (95), 73 (74), 45 (11), 43 (25).

1-(2-Pentyl-phenyl)-ethanone (4m): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (m, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.8 (t, ^3J(H,H) = 7.7 Hz, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.5 (m, 2H), 1.3 (m, 4H), 0.9 (t, ^3J(H,H) = 6.8 Hz, 3H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta =$ 203 (CO), 143–125 (Cs in phenyl group), 34, 32.1, 32, 30, 29.9, 29.8, 29.7, 29.5, 22.8, 14.2; IR (neat): $\tilde{\nu} = 2925$, 2854, 1688 (CO), 1466, 1354, 1251, 950, 758, 600 cm^{-1}; MS: m/z (%): 260 (14) $[M]^+$, 245 (100), 147 (28), 143 (26), 134 (18), 129 (22), 119 (50), 117 (15), 91 (24), 43 (38); HRMS calcd for $C_{13}H_{18}O$ $[M]^+$ 260.214016; found: 260.214069.

1-(2-Pentyl-phenyl)-ethanone (4n): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (m, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.8 (t, ^3J(H,H) = 7.8 Hz, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.6 (m, 2H), 1.3 (m, 4H), 0.9 (t, ^3J(H,H) = 6.8 Hz, 3H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta =$ 203 (CO), 143–125 (Cs in phenyl group), 34, 32, 31.7, 30, 23, 14.2; IR (neat): $\tilde{\nu} = 2952$, 2927, 2857, 1688 (CO), 1456, 1354, 1247, 1071, 800, 758 cm^{-1}; MS: m/z (%): 190 (18) $[M]^+$, 175 (100), 147 (20), 143 (12), 133 (14), 129 (27), 119 (26), 117 (13), 91 (30), 77 (11), 43 (26); HRMS calcd for $C_{13}H_{18}O$ $[M]^+$ 190.135765; found: 190.135876.

1-[2-(2-Methyl-butyl)-phenyl]-ethanone (4p): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.6$ (d, ^3J(H,H) = 7.6 Hz, 1H; Ar), 7.4 (m, 1H; Ar), 7.2 (m, 2H; Ar), 2.9 (m, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.6 (m, 2H), 1.2 (m, 1H), 1.0–0.9 (m, 6H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 203$ (CO), 141–126 (Cs in phenyl group), 40.1, 30, 30.3, 29.6, 19, 11.6; IR (neat): $\tilde{\nu} =$ 1688 cm^{-1} (CO); MS: m/z (%): 190 (14) $[M]^+$, 175 (100); HRMS calcd for $C_{13}H_{18}O$ $[M]^+$ 190.135765; found: 190.136532.

1-(2-Bicyclo[2.2.1]hept-2-yl-phenyl)-ethanone (4q): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.5$ (dd, ^3J(H,H) = 8.1 Hz, 1H; Ar), 7.4 (m, 2H; Ar), 7.2 (m, 1H; Ar), 3.2 (m, 1H(2); *endo*-CH), 2.6 (s, 3H; CH$_3$ to CO), 2.3 (m, 2H; CH(1), CH(4), in norbornyl group), 1.9 (m, 1H(3); *exo*-CH), 1.6 (m, 4H; CH$_2$ in norbornyl group), 1.4 (m, 1H(3); *endo*-CH), 1.2 (m, 2H; CH$_2$ in norbornyl group); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 204$ (C=O), 146–125 (Cs in phenyl group), 53.6, 43.7, 42.8, 40.4, 37.2, 36.8, 30.8, 28.9; IR (neat): $\tilde{\nu} = 2953$, 2870, 1689 (CO), 1598, 1570, 1475, 1354, 1246, 955, 759 cm^{-1}; MS: m/z (%): 214 (52) $[M]^+$, 199 (27), 181 (14), 167 (14), 145 (100), 132 (14), 129 (15), 119 (14), 103 (12), 77 (15), 43 (22); HRMS calcd for $C_{15}H_{18}O$ $[M]^+$ 214.135765; found: 214.135607.

1-[2-(3,3-Dimethyl-butyl)-4-trifluoromethyl-phenyl]-ethanone (4r): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.7$ (d, ^3J(H,H) = 8.5 Hz, 1H; Ar), 7.5 (m, 2H; Ar), 2.8 (m, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.5 (m, 2H; CH$_2$), 1.0 (s, 9H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 201.7$ (CO), 144–122 (Cs in phenyl group), 111.6 (CF$_3$), 46.4, 30.8, 30.3, 29.4, 29.4; IR (solid): $\tilde{\nu} = 2987$, 2869, 1697 (CO), 1473, 1412, 1364, 1333, 1170, 1131, 1090, 958, 830 cm^{-1}; MS: m/z (%): 272 (12) $[M]^+$, 216 (13), 215 (100), 201 (18), 199 (12), 187 (21), 59 (26), 57 (25), 43 (21); HRMS calcd for $C_{15}H_{19}F_3O$ $[M]^+$ 272.138800; found: 272.139267.

1-[2-(3,3-Dimethyl-butyl)-4-methoxy-phenyl]-ethanone (4s): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.7$ (d, ^3J(H,H) = 9.3 Hz, 1H; Ar), 6.7 (m, 2H; Ar), 3.8 (s, 3H; CH$_3$O), 2.9 (m, 2H; ArCH$_2$), 2.6 (s, 3H; CH$_3$ to CO), 1.4 (m, 2H; CH$_2$), 1.0 (s, 9H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 202$ (CO), 162–110 (Cs in phenyl group), 55.5 (CH$_3$O), 46.3, 30.8, 30.4, 29.4, 29.4; IR (neat): $\tilde{\nu} = 2954$, 2866, 1678 (CO), 1603, 1566, 1465, 1355, 1249, 1069, 962, 874 cm^{-1}; MS: m/z (%): 234 (11) $[M]^+$, 219 (14), 178 (13), 177 (100), 163 (11), 161 (15), 91 (5), 43 (13); HRMS calcd for $C_{15}H_{22}O_2$ $[M]^+$ 234.161980; found: 234.161819.

8-(3,3-Dimethyl-butyl)-3,4-dihydro-2H-naphthalen-1-one (13): ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): $\delta = 7.3$ (t, ^3J(H,H) = 7.5 Hz, 1H; Ar) 7.1 (dd, ^3J(H,H) = 7.9 Hz, 2H; Ar) 3.0 (m, 4H), 2.6 (t, ^3J(H,H) = 6.4 Hz, 2H; α-CH$_2$ to CO), 2.1 (qt, ^3J(H,H) = 6.4 Hz, 2H; β-CH$_2$ to CO), 1.4 (m, 2H), 1.0 (s, 9H; CH$_3$); ^{13}C NMR (62.9 MHz, CDCl$_3$, 25 °C): $\delta = 200$ (CO), 147–126 (Cs in phenyl group), 46.2, 41.4, 31.4, 31.0, 30.9, 29.6, 23.2; IR (neat): $\tilde{\nu} =$ 2950, 2866, 1679 (CO), 1591, 1462, 1364, 1321, 1272, 1237, 1212, 760 cm^{-1}; MS: m/z (%): 230 (18) $[M]^+$, 174 (15), 173 (100), 159 (5), 155 (6), 117 (5), 115 (7), 91 (5).

Typical procedure for *o*-alkylation of ketone with olefin: A screw-capped pressure vial (1 mL) was charged with acetophenone (**5a**, 38.9 mg, 0.324 mmol), *tert*-butylethylene (**2a**, 81.6 mg, 0.972 mmol), [RhCl(PPh$_3$)$_3$] (**3**, 15 mg, 0.0162 mmol), benzylamine (17.4 mg, 0.162 mmol), and toluene (0.2 g), and then the mixture was stirred in an oil bath at 150 °C for 6 h. After the resulting ketimine was hydrolyzed by using a HCl solution (1N), the reaction mixture was purified by column chromatography (SiO$_2$, hexanes:ethyl acetate = 5:2) to yield 62.8 mg (95%) of **4a**.

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