

Mechanistic Study of the $\text{Ru}(\text{H})_2(\text{CO})(\text{PPh}_3)_3$ -Catalyzed Addition of C–H Bonds in Aromatic Esters to Olefins

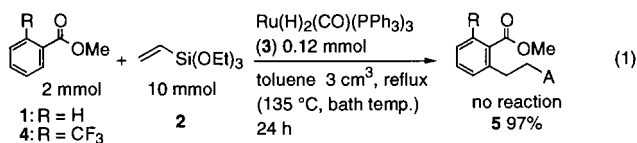
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The reaction mechanism of the $\text{Ru}(\text{H})_2(\text{CO})(\text{PPh}_3)_3$ -catalyzed addition of C–H bonds in aromatic esters to olefins was studied by means of deuterium-labeling experiments and measurement of the ^{13}C kinetic isotope effect. The deuterium-labeling experiment revealed a rapid equilibrium among the intermediates prior to the reductive elimination, and the ^{13}C NMR kinetic isotope effect indicated that C–C bond formation is the rate-determining step in this reaction.

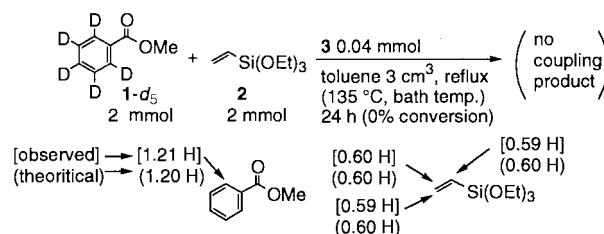
Since the catalytic use of otherwise unreactive C–H bonds via carbon–hydrogen bond cleavage with low-valent transition metal complexes, so called C–H activation, is a subject of considerable interest in organic synthesis,¹ a variety of catalytic reactions, including C–H bond cleavage have been reported by us^{2,3} as well as others.⁴ Most of these studies have focused on exploring the scope and limitations of these types of catalytic reactions and only a few have involved mechanistic aspects.^{3,5–7} We have now studied the mechanism of our catalytic reaction, i.e., the ruthenium-catalyzed aromatic C–H/olefin coupling via chelation-assisted C–H bond cleavage. In this communication, we propose a reaction mechanism, specifically, the rate-determining step, of the $\text{Ru}(\text{H})_2(\text{CO})(\text{PPh}_3)_3$ -catalyzed reaction of aromatic esters with olefins, which was determined by means of an isotope labeling experiment and measurement of the ^{13}C kinetic isotope effect.

We have already noted that when the reaction of methyl benzoate (**1**) with triethoxyvinylsilane (**2**) is carried out in the presence of $\text{Ru}(\text{H})_2(\text{CO})(\text{PPh}_3)_3$ (**3**) as the catalyst, no coupling product was obtained (eq 1).^{2a} In sharp contrast, the introduction of an electron-withdrawing CF_3 group at a position ortho to the ester group resulted in a formation of the coupling product **5** in 97% yield (eq 1).^{2a}



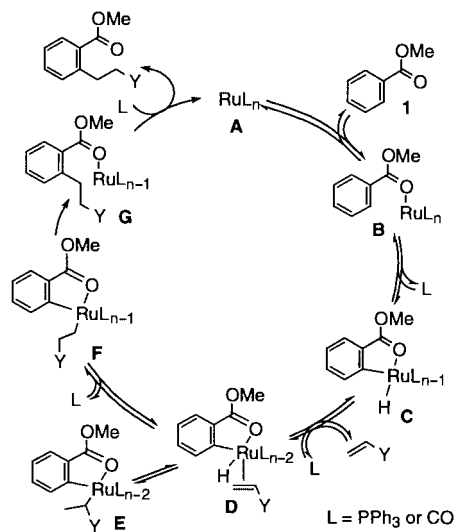
Since the C–H bond dissociation energy is large (ca. 110 kcal/mol; 464 kJ/mol),⁸ one is prone to speculate that the C–H bond cleavage step is rate-determining and that a decrease in the electron density of the C–H bonds as a result of the presence of the electron-withdrawing group enhances the reactivity of the C–H bonds as is often encountered in the case of the oxidative addition of arylhalides to transition metals.⁹ In this case, however, this assumption is not valid. The deuterium labeling experiment described below indicates that the C–H bond cleavage step is not rate-determining. The deuterated substrate, methyl benzoate- d_5 (**1- d_5**), was used for the coupling reaction with **2** (Scheme 1). A GC analysis of the reaction mixture showed that

the starting materials were not consumed after 24 h. An analysis of the recovered starting materials by ^1H NMR spectroscopy revealed that the observed hydrogen intensity at each position was nearly identical to the theoretical value for complete scrambling among the five positions, i.e., two ortho and three olefinic.^{10–12} Very importantly, the observed scrambling of protons provides evidence for the existence of a pre-equilibrium process prior to the reductive elimination.



Scheme 1. H/D exchange reaction between **1- d_5** with **2**.

From the result mentioned above, a plausible reaction mechanism is shown in Scheme 2.¹³ Hydrometalation of the olefin in **D** gives either **E** or **F**. In the present case, **E** can only return to **D** since the branched product was not detected in this reaction. When triethoxyvinylsilane (**2**) was used as an olefin, no C–H/olefin coupling product was obtained. This result indicates that the intermediate **F** does not undergo reductive elimination to give **G**. The deuterium scrambling experiment using **2** (Scheme 1) shows that these equilibrium processes (**A** to **F**) are taking place well ahead of reductive elimination (if any) and suggests that the C–H cleavage is an easy step compared to the product forming process, i.e., the reductive elimination.



Scheme 2. Plausible reaction mechanism.

If C–C bond formation, i.e., the reductive elimination step in this case (**F** to **G** in Scheme 2), is rate-determining, a ^{13}C kinetic isotope effect should be observed at the C6 position.^{14–16} This NMR experiment with ^{13}C at natural abundance was carried out as follows: 1) the catalytic reaction was stopped after an appropriate reaction period (64%, 69%, and 79% conversions); 2) the starting ester was recovered; 3) the relative intensity of the ^{13}C isotope was quantified by the ^{13}C NMR spectrum. If the C–C bond formation step is rate-determining, the relative intensity of the ^{13}C isotope at C6 would be expected to be increased. The reaction of methyl *o*-methylbenzoate with trimethylvinylsilane using **3** as the catalyst was carried out (eq 2). The resulting KIEs ($k_{12}\text{C}/k_{13}\text{C}$) of the aromatic carbons for each conversion are shown in Table 1. The appreciable KIE at C6 (1.033) strongly suggests that C–C bond formation is rate-determining.

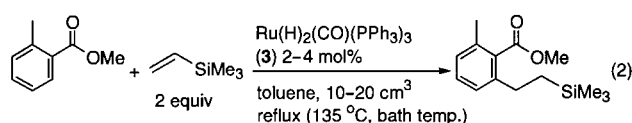
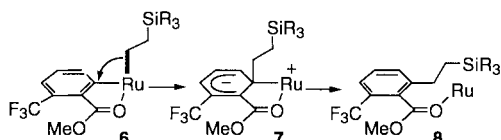


Table 1. Experimental ^{13}C kinetic isotope effect

Run	Conversion	KIEs				
		C1	C2	C3+C4	C5	C6
1	64%	0.996(1)	1.001(3)	1.003(1)	1.000	1.034(1)
2	69%	0.999(2)	0.996(3)	1.000(1)	1.000	1.032(1)
3	79%	0.997(1)	0.996(1)	1.004(1)	1.000	1.034(1)

We have demonstrated that in the $\text{Ru}(\text{H})_2(\text{CO})(\text{PPh}_3)_3$ -catalyzed reaction of aromatic esters with olefins, a rapid equilibrium exists among the intermediates prior to the reductive elimination step and that the C–C bond formation step, i.e., the reductive elimination, is rate-determining but the C–H bond cleavage step is not. Typically, an electron-donating group in the leaving group facilitates reductive elimination.¹⁷ Interestingly, however, in the present case, an electron-withdrawing group, i.e., a CF_3 group, was found to enhance the reactivity of the ester.¹⁸ One possible explanation for this is that an alkyl group on the ruthenium center migrates onto the ortho carbon adjacent to the ruthenium atom (**6** to **7**, Scheme 3). In the case of intermediate **7**, the negative charge generated on the aromatic ring should be stabilized by the electron-withdrawing group. The Ru–C bond in **7** is then cleaved (**7** to **8**, Scheme 3).¹⁹ It should be added that our preliminary study shows that the mechanism of the aromatic ketone and olefin coupling reaction appears to be different from that described here. This will be the subject of future report.



Scheme 3. Two-step mechanism for reductive elimination.

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References and Notes

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- 7 For the reaction mechanism of the rhodium-catalyzed intramolecular hydroacylation of 4-pentenal, see: B. Bosnich, *Acc. Chem. Res.*, **31**, 667 (1998).
- 8 "Handbook of Chemistry and Physics," 71st ed., ed. by D. R. Lide, CRC Press, Boston (1990), pp 9–96.
- 9 For an example, see: M. Portnoy and D. Milstein, *Organometallics*, **12**, 1665 (1993).
- 10 If complete H/D scrambling takes place among the five positions (two ortho positions in **1-d₅** and three vinylic positions in **2**) (Scheme 1), the hydrogen intensity should be 0.60 H (the theoretical value) at each position.
- 11 Supporting information (3 pages) is available on request to the author by telefax (+81-6-6879-7396).
- 12 We also observed H/D scrambling between **1-d₅** and triethylvinylsilane under reaction conditions similar to those shown in Scheme 1. This result indicates that the substituent on the silicon atom does not affect the rate-determining step.
- 13 Kinetics of this catalytic reaction should be studied, in order to discuss the reaction mechanism completely. In some preliminary studies, we observed that, in the case of the reaction of methyl *o*-methylbenzoate, two molecules of olefin would be expected to participate in the rate-determining step of this catalytic reaction. The determination of the actual mechanism of this reaction awaits further investigation.
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- 18 We did not measure the ^{13}C KIEs for the reaction of **4** because the splitting of each aromatic carbon by ^{13}C – ^{19}F spin–spin coupling resulted in low accuracy of the quantification of the ^{13}C abundance. However, when a reaction of **4** with triethylvinylsilane- d_3 ($\text{CD}_2=\text{CDSiEt}_3$) was carried out, H/D scrambling was observed. From this observation, we believe that the C–C bond formation step is also rate-determining.
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