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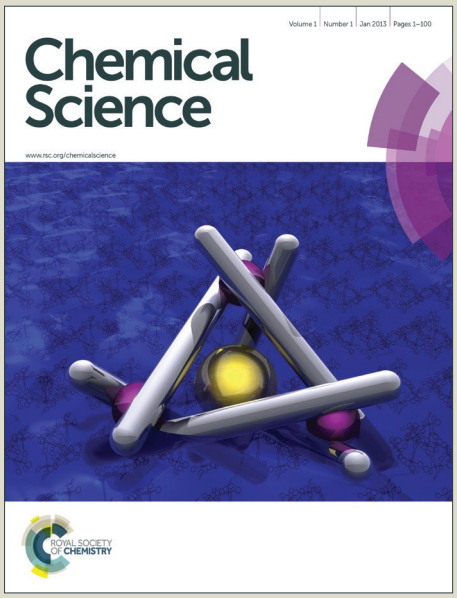

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ARTICLE

Mechanistic Study of Rhodium-Catalyzed Carboxylation of Simple Aromatic Compounds with Carbon Dioxide

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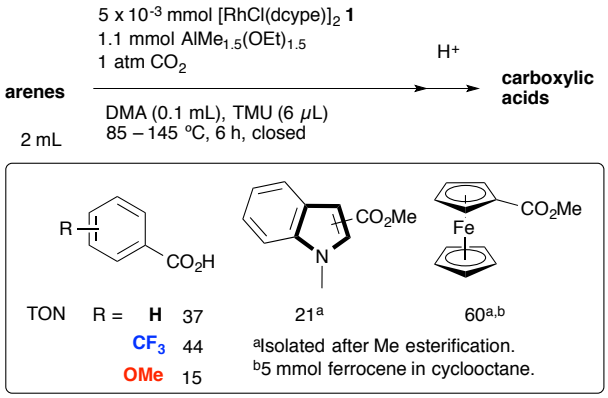
The detailed mechanism of Rh(I)-catalyzed carboxylation of simple aromatic compounds via C–H bond activation was investigated. Kinetic studies with model compounds of the postulated key intermediates revealed that 14-electron complexes RhMe(dcype) and RhPh(dcype) participated in the C–H bond activation step and the carboxylation step, respectively. Interestingly, undesired carboxylation of RhMe(dcype) to give acetic acid was found to be much faster than the desired C–H bond activation reaction under the stoichiometric conditions, however, C–H bond activation reaction could occur under the catalytic conditions. Careful controlling experiments revealed that C–H bond activation by the RhMe(dcype) became competitive with its direct carboxylation under the conditions that the concentration of CO_2 in the liquid phase was rather low. This factor could be controlled to some extent by mechanical factors such as the stirring rate and the shape of the reaction vessel. The resting state of the rhodium species under catalytic conditions was found to be $[RhCl(dcype)]_2$, and the proposed intermediates such as RhMe(dcype) and Rh(OAc)(dcype) were readily converted to the most stable $[RhCl(dcype)]_2$ via transmetallation with [Al]–Cl species, thus preventing the decomposition of the active catalytic species.

Introduction

Catalytic direct carboxylation of simple hydrocarbons with carbon dioxide (CO_2) is a formidable challenge in organic chemistry.[1] Recently, we reported Rh(I)-catalyzed carboxylation of simple aromatic compounds such as benzene and toluene by using a combination of $[RhCl(dcype)]_2$ **1** (dcype: 1,2-bis(dicyclohexylphosphino)ethane) and $AlMe_{1.5}(OEt)_{1.5}$ as a stoichiometric methylating agent (Scheme 1).[2-4] The most attractive feature of this reaction is its wide generality. Not only electron poor/rich arenes, but also heteroaromatics such as benzofuran and indole were carboxylated successfully. Furthermore, ferrocene showed remarkable reactivity in this reaction.



Scheme 1 Rh-catalyzed C–H bond carboxylation.

The proposed reaction mechanism is shown in Scheme 2. The reaction starts with generation of a 14-electron methylrhodium(I) complex **A** by transmetallation of $[RhCl(dcype)]_2$ **1** with $AlMe_{1.5}(OEt)_{1.5}$ followed by oxidative addition of an sp^2 C–H bond of benzene to **A**, giving phenyl(hydrido)(methyl)rhodium(III) intermediate **B**. Reductive elimination of methane from **B** affords a reactive 14-electron phenylrhodium(I) complex **C**.[5] Nucleophilic addition of **C** to CO_2 gives a rhodium(I) benzoate complex **D**,[6] which is converted to methylrhodium(I) **A** through transmetallation with $AlMe_{1.5}(OEt)_{1.5}$.

The key of our success consists of three main factors. The first one is the choice of methylrhodium(I) as the C–H activation species. It was reported as a stoichiometric reaction by Andersen's and Field's groups that heating or photoirradiating methylrhodium(I) species in benzene afforded corresponding phenylrhodium(I) species.[5] It was expected that by using methylrhodium(I) species, the irreversible dissociation of methane from intermediate **B** would give the desired arylrhodium(I) species efficiently. The second one is the reactivity of RhMe(dcype) **A**. For the success of the preparation of benzoic acid, direct carboxylation of **A** to produce acetic acid should be slower than the C–H bond activation of benzene by **A**. If the direct carboxylation was much faster than the C–H bond activation, the reaction would

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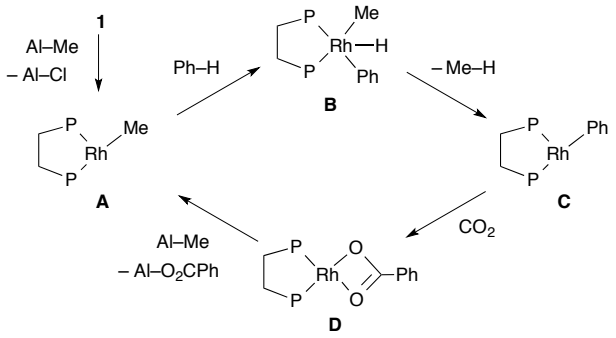


Scheme 2 Postulated reaction mechanism.

produce acetic acid only. The third one is the choice of the methylating agent to regenerate **A**. Methylaluminum was selected because it is well-known to be reactive for transmetallation, but it does not directly react with CO_2 under appropriate conditions. Other reagents such as MeMgBr are unsuitable for this reason.

Apart from the synthetic utility, the noteworthy feature of this reaction is the realization of C–H bond activation followed by nucleophilic addition by using a combination of a low-valent transition metal catalyst and a stoichiometric alkylating agent. Such C–H bond functionalization strategies are quite limited and most of the reported C-H activation–nucleophilic addition reactions utilize high-valent transition metal complexes such as Rh(III) for C-H bond activation.[7] In 2010, we reported the first example of such reaction, that is, rhodium-catalyzed direct carboxylation of 2-phenylpyridines.[8] In 2012, Yoshikai reported a catalytic C–H bond activation of 2-phenylpyridine derivatives using a combination of a cobalt catalyst and stoichiometric organomagnesium reagent, followed by nucleophilic addition to *N*-arylimines.[9] Very recently, Wang reported the use of a manganese catalyst with a stoichiometric amount of dimethylzinc was effective to the coupling of 2-phenylpyridines with aldehydes and nitriles.[10,11] This kind of catalytic nucleophilic addition is still limited, but would become a powerful methodology in C–H bond functionalization reactions.

As described above, several reactions have recently been reported for this type of C-H activation–nucleophilic addition reactions, however, there has been almost no detailed study on the mechanism of such reactions, probably because of the difficulty in capturing highly reactive alkyl or aryl transition metal intermediates. For example, confirmation of the intermediacy of 14-electron complex in C–H activation and carboxylation step is not necessarily easy in our reaction because of their instability. As already described, stoichiometric reactivity of relevant methylrhodium(I) species to C–H bond activation has been known for more than three decades, but its detailed mechanistic study has not been carried out.[5] Concerning the carboxylation step, there are several reports for stoichiometric carboxylation reactions of arylrhodium(I) complexes,[6] however, their mechanisms have been proposed only by theoretical studies.[12] Furthermore, transmetallation behaviors and the resting state are also left unclarified. In this paper, we report detailed analysis of the mechanism of this rhodium-catalyzed C–H carboxylation reaction based on kinetic studies using several model compounds, examination of various reaction conditions including the shape of the reaction vessels and the stirring rate, analysis of the reaction mixture, and some controlling experiments.

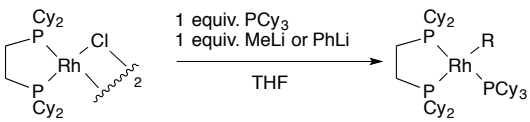
Results and discussion

1: Preparation and reactivity of tetracoordinated 16-electron rhodium species

To support the proposed reaction mechanism shown in Scheme 2, we initially tried to prepare each intermediate in the proposed catalytic cycle. In particular, 14-electron complexes RhMe(dcype) **A** and RhPh(dcype) **C** were the most attractive because they were thought to be the true intermediates in the most important C–H bond activation and carboxylation steps.

Tricoordinated 14-electron alkylrhodium complexes are known to be so unstable that they had not been isolated except for few specific examples.[13] Indeed, we initially attempted to prepare them by treatment of $[RhCl(dcype)]_2$ **1** with several methylating agents such as methyllithium, methylmagnesium bromide and trimethylaluminum, however, all efforts turned out to be fruitless. Therefore, we decided to prepare tetracoordinated 16-electron complexes RhMe(PCy_3)(dcype) **2** and RhPh(PCy_3)(dcype) **3** as appropriate precursors of 14-electron complex (Scheme 3).[14] **2** and **3** were prepared in good yields by treatment of $[RhCl(dcype)]_2$ with MeLi and PhLi, respectively in the presence of a stoichiometric amount of PCy_3.[15] Their structures were determined by ^1H and ^{31}P NMR. **3** was also characterized by single crystal X-ray structure analysis (see SI).

Next, the reactivity of these complexes for C–H bond activation and carboxylation reaction was examined. To our delight, RhMe(PCy_3)(dcype) **2** was found to react with benzene to give RhPh(PCy_3)(dcype) **3** under argon at 85 ºC with perfect conversion although partial decomposition was also observed (Scheme 4). Moreover, further exposure of this solution to 1 atm CO_2 at 85 ºC gave a mixture of carboxylated products Rh(O_2CPh)(dcype) **D** and Rh(O_2CPh)(PCy_3)(dcype) **D'** (**D** : **D'** = 1 : 2 at room temperature). No intermediates were observed in these two reactions. The rhodium benzoates were characterized by comparing their ^{31}P NMR spectra with those of authentic samples **D** and **D'** (see SI for their preparative methods).



Scheme 3 Preparation of model complexes.

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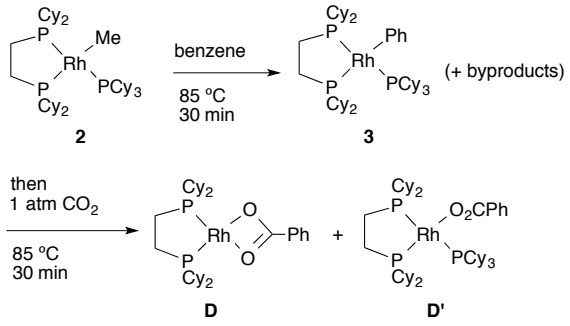
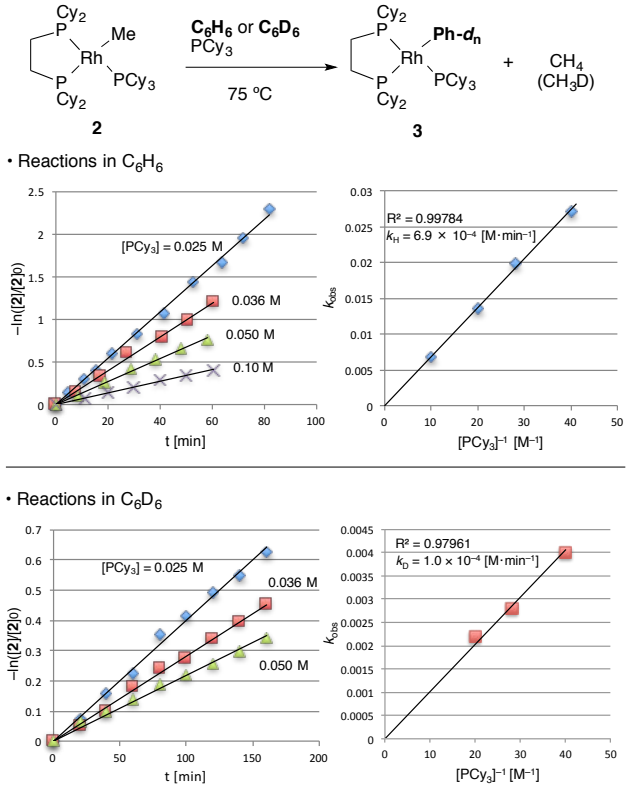


Scheme 4 Reactions of model complexes.[a]

2. Mechanistic study on C–H bond activation by methylrhodium(I) species

With the suitable model complexes in hand, we carried out kinetic study of the C–H bond activation step by monitoring the reaction with ^{1}H NMR (Figure 1). The rate of the C–H bond activation reaction of RhMe(PCy_3)(dcype) **2** with solvent benzene-d_0 was measured in the presence of various concentrations of PCy_3. Fortunately, the addition of PCy_3 completely suppressed decomposition of the complex, and the desired transformation proceeded quantitatively according to the ^{31}P NMR spectra (see SI).[16] The reaction was found to be first order to RhMe(PCy_3)(dcype) **2** and inverse first order to PCy_3 (eq.1).



Conditions: 0.005 mmol **2**, 0.50 mL benzene in NMR tube under argon. The reaction was analyzed by ^{1}H NMR. Consumption of **2** was traced with decay of the signal at $\delta = 0.4$ ($RhCH_3$). No other products were observed in ^{31}P NMR after the reactions.

Fig. 1 Kinetics of C–H bond activation.

$$-\ln([\mathbf{2}]/[\mathbf{2}]_0) = k_{H(D)}[PCy_3]^{-1}\,t \qquad (1)$$

$$k_H = 6.9 \times 10^{-4}\ [M \cdot min^{-1}]$$

$$k_D = 1.0 \times 10^{-4}\ [M \cdot min^{-1}]$$

$$k_H/k_D = 6.9$$

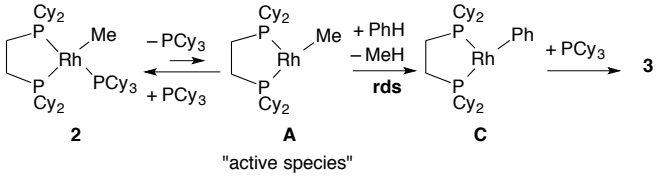
The value of $-\ln([\mathbf{2}]/[\mathbf{2}]_0)$ was completely proportional to the reaction time even after 90 % conversion, and was inversely proportional to [PCy_3] with the rate constant k_H = 6.9 x 10^{-4} [M·min^{-1}] at 75 ºC. According to steady state approximation, this reaction includes dissociation of PCy_3 before the rate-determining step. In addition, the reaction in benzene-d_6 was apparently slower (k_D = 1.0 x 10^{-4} [M·min^{-1}]) than in benzene-d_0 and the KIE value (k_H/k_D) was estimated to be 6.9. This large KIE value strongly suggests C–H bond activation step is rate-determining in this stoichiometric reaction.

With these results, it was concluded that tricoordinated RhMe(dcype) **A** is the true intermediate of the C–H bond activation step (Scheme 5). ^{1}H NMR analysis also indicated formation of CH_4 in benzene-d_0, and CH_3D in benzene-d_6. The detailed process of C–H bond activation remains unclear by our study, but oxidative addition–reductive elimination process should be the most plausible. For instance, Sakakura reported photo-induced reaction of $Rh^{I}Cl(PMe_3)_3$ in benzene generated $Rh^{III}(H)(Cl)(Ph)(PMe_3)_3$.[17,18]

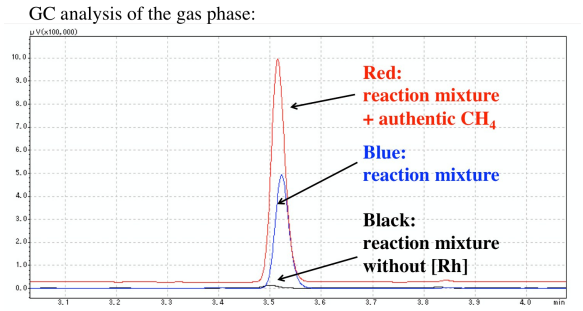
The formation of methane was also confirmed by GC analysis of the reaction mixture under catalytic conditions (Figure 2). After the catalytic carboxylation of benzene was carried out under optimized conditions by using [RhCl(dcype)]$_2$ **1** and $AlMe_{1.5}(OEt)_{1.5}$, the gas phase of the resulting mixture was directly injected to GC. While no methane formation was observed in the absence of [RhCl(dcype)]$_2$ **1**, it was detected under catalytic conditions.

We also carried out several KIE studies *under the catalytic conditions* to determine the turnover-limiting step. It should be noted that accurate kinetic study of this reaction is difficult under our conditions because of the CO_2 concentration problem (noted in the later section) and a complex disproportionation of methylaluminum reagent. Therefore, the results described below may not be very precise but are sufficient for the general discussions.

The KIEs were measured by two procedures (Scheme 6). In procedure 1, the reaction was performed using a 1 : 1 mixture of benzene-d_0 and benzene-d_6. In procedure 2, the reactions of benzene-d_0 and benzene-d_6 were carried out in separate vessels, and the resulting mixtures were combined after quenching the reaction with aqueous 1M HCl. Both reactions were performed at 85 ºC for 1 h. The ratio of benzoic acid-d_0



Scheme 5 Plausible pathway of C–H bond activation step.



[a]The reaction was carried out in benzene at 85 ºC. Detailed reaction conditions were the same as shown in Scheme 1.

Figure 2 Methane observation by GC analysis[a].

and benzoic acid-d_5 was estimated by ^{1}H NMR after esterification of benzoic acids with benzyl bromide. As a result, [**5-d_0**]/[**5-d_5**] = 5.5 (conditions 1) and [**5-d_0**]/[**5-d_5**] = 4.0 (conditions 2) were obtained, respectively. These large KIE values indicate that the C–H bond activation step is the turnover-limiting also under the catalytic conditions.

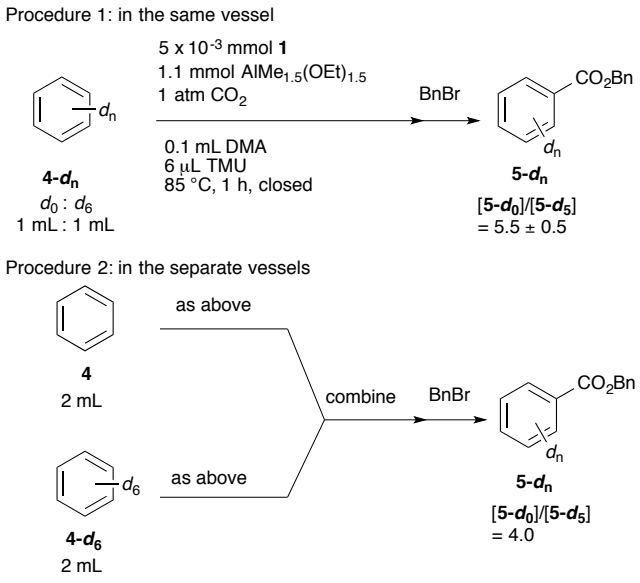
3. Mechanistic study on the carboxylation step

Next, the kinetic study of the carboxylation reaction of RhPh(PCy$_3$)(dcype) **3** was carried out under CO_2 (1 atm at 22-23 ºC) in the presence of PCy$_3$ in toluene-d_8 (Figure 3).[19] The value of –ln([**3**]/[**3**]$_0$) was proportional to the reaction time and was almost inversely proportional to [PCy$_3$] with the rate constant k_{Ph1} = 2.5 x 10^{-3} [M·min^{-1}] at 35 ºC (eq. 2), suggesting that the carboxylation step is much faster than the C–H activation step, which coincided with the results of KIE studies.

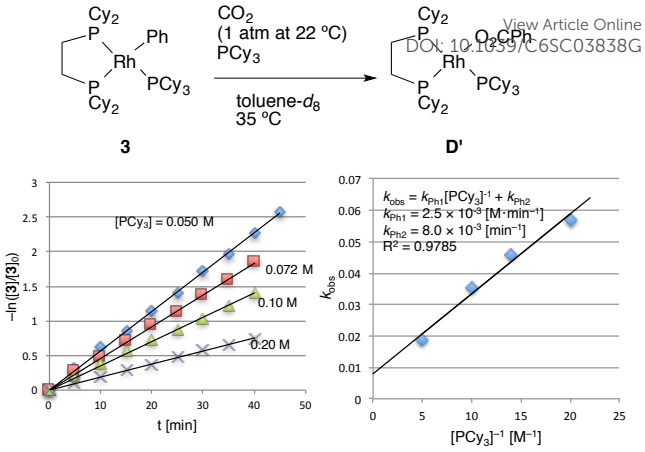
$$-\ln([\mathbf{3}]/[\mathbf{3}]_0) = (k_{Ph1}[PCy_3]^{-1} + k_{Ph2})\,t \qquad (2)$$

$$k_{Ph1} = 2.5 \times 10^{-3}\ [\mathrm{M \cdot min^{-1}}]$$

$$k_{Ph2} = 8.0 \times 10^{-3}\ [\mathrm{min^{-1}}]$$



Scheme 6 KIE study under catalytic conditions.



Conditions: 0.005 mmol **3**, 0.50 mL toluene-d_8 in NMR tube (ca. 4 mL vol.) under 1 atm CO_2. The solution was saturated with CO_2 at 22-23 ºC beforehand (see SI). Consumption of **3** was traced with decay of the signal at δ 7.9 ppm (Ph). No other products were observed in ^{31}P NMR after the reactions.

Fig. 3 Kinetics of carboxylation of **3**.

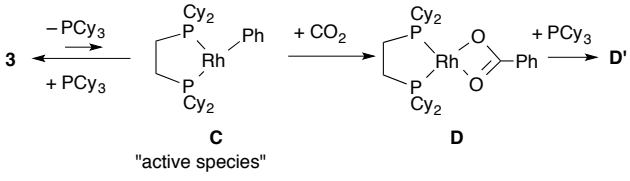
Dissociation of PCy$_3$ was clearly involved also in the carboxylation step. The small intercept term k_{Ph2} = 8.0 x 10^{-3} [min^{-1}] left a possibility of a minor pathway (e.g. the reaction without dissociation of PCy$_3$), but it was trivial at lower concentration of PCy$_3$. Therefore, it is concluded that the carboxylation step mainly proceeded via 14-electron complex RhPh(dcype) **C** in a similar manner to the C–H bond activation step (Scheme 7).

The carboxylation reaction of RhMe(PCy$_3$)(dcype) **2** was also carried out in toluene-d_8 at 35 ºC (Figure 4).[20] **2** showed somewhat lower reactivity of carboxylation compared to RhPh(PCy$_3$)(dcype) **3** (eq.3, k_{Me1} = 1.0 x 10^{-3} [M·min^{-1}] vs k_{Ph1} = 2.5 x 10^{-3} [M·min^{-1}]).

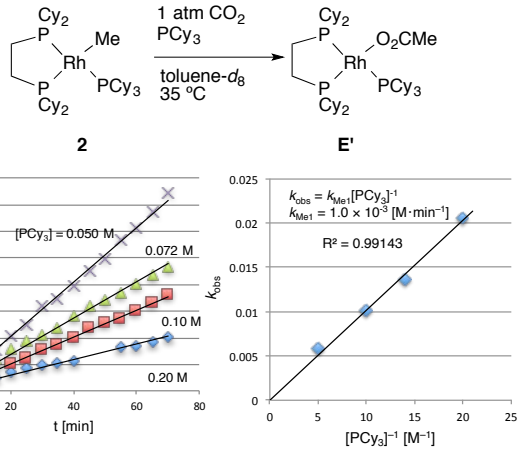
$$-\ln([\mathbf{2}]/[\mathbf{2}]_0) = k_{Me1}[PCy_3]^{-1}\,t \qquad (3)$$

$$k_{Me1} = 1.0 \times 10^{-3}\ [\mathrm{M \cdot min^{-1}}]$$

The equation was similar to that of RhPh(PCy$_3$)(dcype) **3** except complete disappearance of the intercept term (k_{Me2} = 0), suggesting intermediacy of RhMe(dcype) **A** as a reactive species. ^{1}H and ^{31}P NMR indicated no formation of C–H activation product Rh(tol)(PCy$_3$)(dcype) or corresponding benzoates throughout the reaction. In addition, the stoichiometric reaction of RhMe(PCy$_3$)(dcype) **2** under 1 atm CO_2 in benzene at 85 ºC did not give benzoates at all, but gave only acetates Rh(OAc)(dcype) **E** and Rh(OAc)(PCy$_3$)(dcype) **E'** (Scheme 8). These results imply carboxylation of RhMe(dcype) **A** with CO_2 proceeded much faster than C–H activation of **A**



Scheme 7 Plausible pathway of carboxylation step.



Conditions: 0.005 mmol **2**, 0.50 mL toluene-d_8 in NMR tube (ca. 4 mL vol.) under 1 atm CO_2. The solution was saturated with CO_2 at 22-23 ºC beforehand (see SI). Consumption of **2** was traced with decay of the signal at δ 0.4 ppm (CH_3).

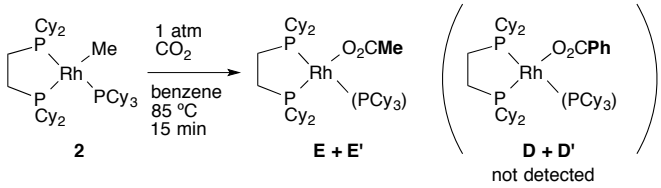
Fig. 4 Kinetics of carboxylation of **2**.

with benzene under 1 atm CO_2. In other words, predominant formation of acetic acid should associate with formation of benzoic acid.

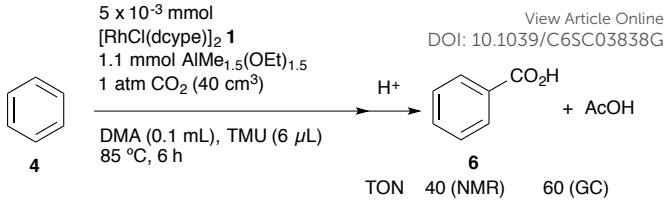
Based on the above consideration, TON of acetic acid (AcOH) was estimated by GC analysis under the catalytic conditions. According to the standard catalytic procedure, the reaction was carried out in 40 cm^3 test tube for 6 h at 85 ºC with the tube kept closed. As we expected, it was found that in addition to ca. 0.40 mmol (TON = 40) of benzoic acid, ca. 0.6 mmol (TON = ca. 60) of acetic acid was produced as judged by GC analysis (Scheme 9). However, the ratio of BzOH : AcOH = 2 : 3 was still inconsistent with the result of the stoichiometric study. To obtain more information on the competitive formation of benzoic acid and acetic acid, we decided to carry out more detailed analysis of the reactions to clarify the difference of these stoichiometric and catalytic reactions.

All the reactions so far have been carried out using 40 cm^3 test tube (ca. 2 mmol of CO_2 should be inside) in a closed system for the catalytic reaction, and ca. 1 mmol of CO_2 was consumed to produce benzoic acid and acetic acid as shown in Scheme 9. As the amount of CO_2 in the reaction mixture was thought to be influential on the ratio of carboxylic acids under the catalytic conditions, the reaction was examined using several apparatuses with different shape and volume.

The effect of the reaction apparatus was examined by changing the total volume of the apparatus and/or the shape of the reaction vessel (Table 1).[21] The reaction time was set to



Scheme 8. Stoichiometric Carboxylation of **2** at 85 ºC.

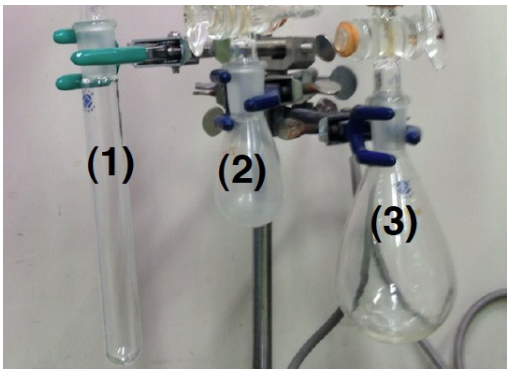


Scheme 9 Confirmation of acetic acid formation.

1 h to reduce effects of catalyst decomposition and reagent consumptions. The stirring rate was kept ca. 800 rpm. The reaction apparatuses were; a 40 cm^3 test tube (ø = 2 cm, vessel 1) with a closed system (entry 1), a 40 cm^3 test tube (vessel 1) with a 2000 cm^3 balloon filled with CO_2 to disregard the decrease of CO_2 in a whole vessel (entry 2), a 40 cm^3 round-bottom flask (vessel 2) with a 2000 cm^3 balloon (entry 3) and a 160 cm^3 round-bottom flask (vessel 3) with a closed system (entry 4). In entry 4, the content of CO_2 should also be sufficient (ca. 7 mmol).

It was found that the volume of the apparatus was not so influential on the ratio of benzoic acid and acetic acid, but the shape of the vessel caused a dramatic difference. The value of [BzOH]/[AcOH] in vessel 1 was 0.12 without a balloon and 0.14 with a balloon (entry 1 vs 2). It indicated the total content of CO_2 was not responsible for the selectivity in initial 1 h of the reaction time.[22] In sharp contrast, the use of vessel 2 decreased [BzOH]/[AcOH] to 0.03 (entry 2 vs 3). The formation of acetic acid was predominant when vessel 3 was employed (entry 4, [BzOH]/[AcOH] = 0.01) as observed in the reaction of RhMe(PCy_3)(dcype) **2** under CO_2 in benzene (Scheme 8).

Table 1 Effect of CO_2 content and the shape of the vessel.[a]



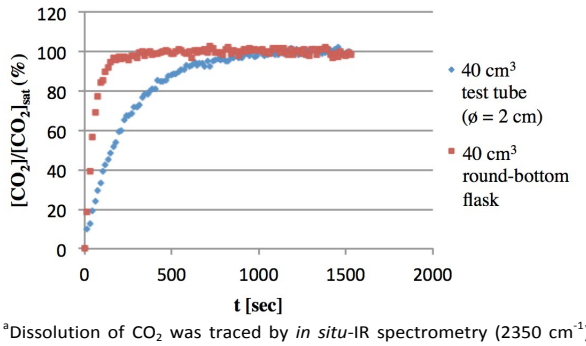
entry	conditions	total volume (cm^3)	TON		[BzOH]/[AcOH]
			[BzOH]	[AcOH]	
1	vessel 1	40	7.9	68	0.12
2	vessel 1 + balloon	40+2000	5.7	42	0.14
3	vessel 2 + balloon	40+2000	2.5	84	0.03
4	vessel 3	160	1.3	147	0.01

[a]Vessel 1: a 40 cm^3 test tube (ø = 2 cm), Vessel 2: a 40 cm^3 round-bottom flask, Vessel 3: a 160 cm^3 round-bottom flask. Conditions were shown in Scheme 9, except that the reaction time was shortened to 1 h. Stirring rates were approx. 800 rpm.

This large effect of the shape of the vessel would be due to the dissolution rate of CO_2 into solution, which was elucidated by *in situ*-IR analysis at room temperature (Figure 5).[23] CO_2 dissolution occurred more rapidly in a 40 cm^3 round-bottom flask than in a 40 cm^3 test tube even though they have almost the same total volume. For instance, the CO_2 concentration reached saturation within 200 seconds in the round-bottom flask. On the other hand, it took almost 1000 seconds in the test tube. Although the results shown here were obtained without stirring, the rate of dissolution of CO_2 certainly depends on the surface area of the solution, which influenced the ratio of BzOH and AcOH. For the same reason, the stirring rate was also found to be responsible (Table 2). The slower stirring gave an improved ratio of [BzOH]/[AcOH], although total TON decreased. For example, [BzOH]/[AcOH] was 0.25 and total TON was 41 at 100 rpm, while [BzOH]/[AcOH] was 0.07 and total TON was 99 at 1000 rpm.

From these results, it was concluded that this reaction strongly depends on CO_2 concentration in the liquid phase, which was mainly determined by the dissolution rate of CO_2. In other words, the liquid phase is not saturated with CO_2 owing to its fast consumption by carboxylation reactions under catalytic conditions. In the presence of sufficient CO_2, intermediate RhMe(dcype) **A** mostly reacts with CO_2 to give acetic acid before it reacts with benzene to give RhPh(dcype) **C** as observed in entry 4 in Table 1 and entry 3 in Table 2, and it agrees with the result of the *stoichiometric* reaction of RhMe(PCy_3)(dcype) **2** in CO_2-saturated benzene. However, the true concentration of CO_2 should be rather low under *catalytic* conditions particularly with slower stirring and a liquid phase with a smaller surface area. Then, carboxylation and C–H bond activation of benzene by RhMe(dcype) **A** becomes competitive under such conditions, and both benzoic acid and acetic acid were obtained catalytically in contrast to the stoichiometric reaction of RhMe(PCy_3)(dcype) **2**.

In summary, we proved 14-electron tricoodinated RhPh(dcype) **C** is a plausible intermediate in the carboxylation step. RhMe(dcype) **A** also reacted with CO_2 in a similar way to give acetic acid catalytically. This undesired pathway was predominant over desired C–H bond activation reaction under 1 atm CO_2. Nevertheless, C–H bond activation of benzene took place successfully under the catalytic conditions because the concentration of CO_2 in the liquid phase was much lower than saturation due to its consumption by the carboxylation reaction of RhMe(dcype) **A**. Thus, dissolution rate of CO_2 controlled the fate of the key intermediate RhMe(dcype) **A**. It clearly indicates the balance between C–H bond activation and the subsequent transformation is very important for the catalytic C–H bond functionalization reaction using these alkyl metal complexes.



[a]Dissolution of CO_2 was traced by *in situ*-IR spectrometry (2350 cm^{-1}) in 2 cm^3 toluene at room temperature. The mixtures were stood without stirring during measurements.

Fig. 5 Dissolution of CO_2 in toluene.[a]

Table 2 Effect of stirring rate.

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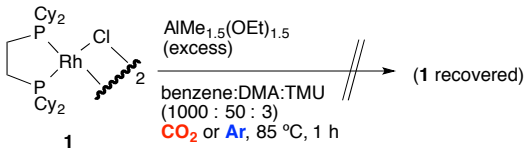
entry	rate [rpm]	TON [BzOH]	TON [AcOH]	[BzOH]/[AcOH]
1	100	8.3	33	0.25
2	800	7.9	68	0.12
3	1000	6.2	93	0.07

Reactions were carried out in 40 cm^3 test tubes (closed system). Conditions were the same as noted in Table 1.

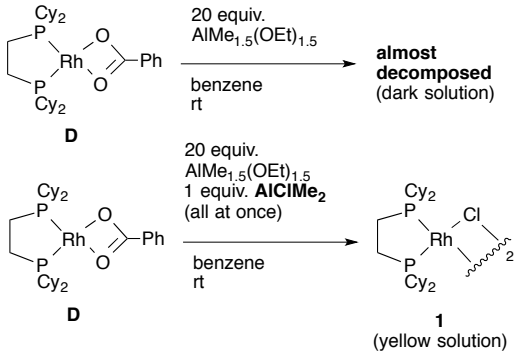
4. Transmetallation Behaviors

Direct observation of the reaction mixture is a reliable method to obtain information on the resting state of the catalytic cycle. We then observed ^{31}P NMR to clarify the rhodium species present in the reaction mixture after the catalytic reaction was carried out in benzene for 1 h under 1 atm CO_2 at 85 ºC (Scheme 10). It was a surprise to find that almost no complex except for the starting $[RhCl(dcype)]_2$ **1** was observed even though benzoic acid was produced gradually. Alternatively, only **1** was observed under argon also. No methylrhodium or phenylrhodium species were observed. $[RhCl(dcype)]_2$ **1** mostly decomposed after 6 h of heating under Ar. Therefore, it was speculated that there would be equilibria between **A**-**D** to **1**, so that only **1** was observable.

To confirm our speculation, Rh(O_2CPh)(dcype) **D** was prepared and its catalytic activity was examined. When the catalytic carboxylation reaction of benzene was carried out using **D** as a catalyst, benzoic acid was obtained in TON of only 2.5. In addition, when **D** and excess $AlMe_{1.5}(OEt)_{1.5}$ were mixed in benzene at room temperature (no chloride source), rapid decomposition of the complex was observed by ^{31}P NMR (Scheme 11). However, it was found that addition of only an equimolar amount of $AlClMe_2$ to **D** prevented it from decomposition to give $[RhCl(dcype)]_2$ **1**, and the catalytic activity was recovered (TON 28). In other words, the success of the present reaction was due to the fast transmetallation of rather unstable [Rh]-O_2CPh or [Rh]-Me with [Al]-Cl to give stable dimeric [Rh]-Cl species under the catalytic conditions.

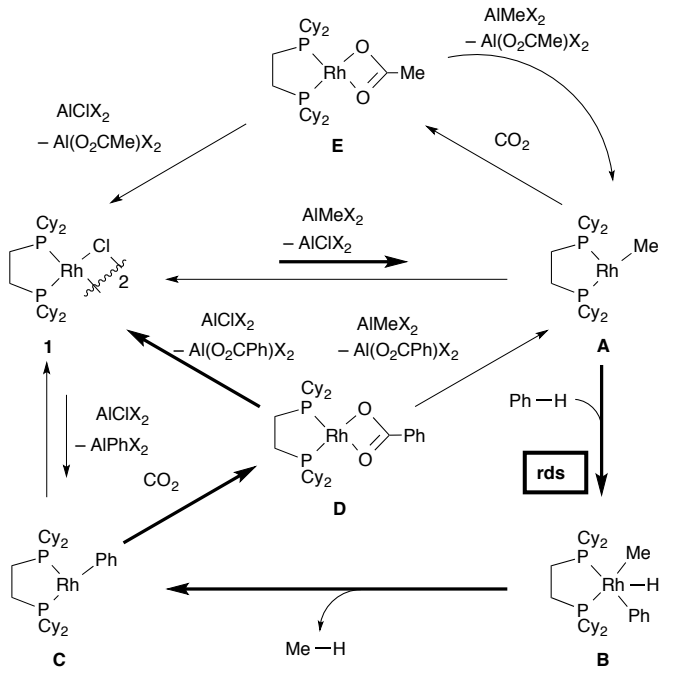


Scheme 10 Analysis of the reaction mixture by ^{31}P NMR.



Scheme 11 Transmetallation of Rh–O_2CPh complex.

The total figure of this reaction is illustrated in Scheme 12. The most important cycle, which provides benzoic acid, is confirmed to be fundamentally the same as we postulated (depicted in bold arrows). First, transmetallation of $[RhCl(dcype)]_2$ **1** and $AlMe_{1.5}(OEt)_{1.5}$ generates 14-electron methylrhodium complex RhMe(dcype) **A**. **A** reacts with benzene to give 14-electron phenylrhodium complex RhPh(dcype) **C**, possibly via reductive elimination of methane from Rh(H)(Me)(Ph)(dcype) **B**. The following carboxylation of **C** provides rhodium benzoate Rh(O_2CPh)(dcype) **D**. There are two possible pathways in the next step. Transmetallation of **D** and chloroaluminum species converts back the catalyst to $[RhCl(dcype)]_2$ **A**, or transmetallation of **D** and methylaluminum species directly gives RhMe(dcype) **A**. However, generated **A** could be converted to the most thermodynamically stable **1** via further transmetallation because of an equilibrium between **1** and **A**.[24,25] In addition, there is a branch in this reaction. **A** reacts with CO_2 to give Rh(OAc)(dcype) **E** in the same manner as **C**. Therefore, this reaction provides a mixture of acetic acid and benzoic acid.



Scheme 12 Total figure of the catalytic cycle.

The undesired formation of **E** should be operative if the reaction mixture contains sufficient amount of CO_2 in solution. Nevertheless, the desired C–H bond activation takes place because the true concentration of CO_2 in solution is much lower than saturation. Importantly, the catalytic reaction did not work well in the absence of the chloride source. This is probably because tricoordinated active species RhMe(dcype) **A** was too unstable to be present in higher concentration and decomposition of the Rh species occurred. The presence of chloride species keeps the resting state of the rhodium species as $[RhCl(dcype)]_2$ **1**, which has stable tetracoordinated dimeric structure and moderately reactive to transmetallation with Al-Me species. This equilibrium limited the concentration of active species RhMe(dcype) **A** and suppressed its decomposition. Transmetallation steps have attracted less interest in mechanistic studies, and their possible equilibria are mostly ignored. Our observation should be an interesting example to show the importance of the transmetallation equilibria in the catalytic cycle.

Conclusions

This article described a detailed mechanistic analysis of rhodium-catalyzed carboxylation of simple aromatic compounds. Although no active intermediates were observable at all in this reaction, the proposed mechanism was mostly supported by several experiments. Most importantly, elucidation of the active species was achieved by designing appropriate precursors and the following kinetic studies. 14-electron rhodium complexes were found to be the key intermediates in both of C–H bond activation and carboxylation steps. The presence of such species was also supported by the formation of methane and acetic acid. KIE study under the catalytic conditions revealed that the C–H bond activation step was the turnover-limiting step. According to the kinetic studies, this C–H bond activation step should be a minor pathway in the presence of a sufficient amount of CO_2 because of undesired predominant carboxylation of Rh^I-Me species. However, further analysis revealed that this problem could be overcome to some extent by mechanical factors such as stirring rate and the shape of the reaction vessel, because undesired carboxylation of Rh^I-Me species could be made slower by controlling the concentration of CO_2 in solution. Finally, it was found that the reversible transmetallation pathways to give $[RhCl(dcype)]_2$ **1** contributed to suppress decomposition of the catalyst. This study will provide a new possibility in such C–H bond functionalization reactions using alkyl-metal species and transition metal-catalyzed carboxylation reactions.

Acknowledgements

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19 Insufficient introduction of CO_2 led to irreproducible results. See SI for the practical experimental procedure.

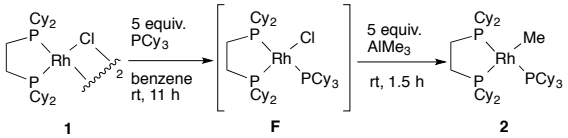
20 According to ^{31}P NMR analysis, the reaction mixture included a small amount of Rh(OAc)(dcype) **E** at lower concentration of PCy_3 and it affected concentration of free PCy_3. But it was trivial so that linear correlation was mostly maintained throughout the experiment.

21 It should be noted that we used Chemistation™ (Tokyo Rikakikai Co. Ltd.) for heating a reaction mixture in other experiments including Scheme 9. This apparatus cools the system just above the liquid phase to maintain gentle refluxing. On the other hand, experiments in Table 1–3 were carried out in an oil bath, which does not have a cooling system for a practical reason. Such small difference also affected the results. For example, TONs of BzOH and AcOH were 15 and 54 respectively, when the reaction in entry 1 (Table 1) was carried out using Chemistation™.

22 Decrease of CO_2 should affect the results in longer reaction time. The amount of acetic acid in Scheme 9 (TON = 60) suggests acetic acid does not form so much at the later stage of the reaction.

23 The experiments at higher temperature were unsuccessful owing to the sensitivity of our equipment.

24 Addition of an appropriate ligand enables observation of methylrhodium(I) complex in such Rh-Cl/Al-Me transmetallation equilibrium. For example, the reaction of $RhCl(PCy_3)$(dcype) **F** with $AlMe_3$ gave $RhMe(PCy_3)$(dcype) **2** as a major product. Interestingly, use of $AlMe_{1.5}(OEt)_{1.5}$ resulted in no reaction under the similar conditions. These results might have relation with the better results obtained using the latter reagent in the carboxylation reaction.[2]



1 F 2

25 There would also be an equilibrium between **1** and RhPh(dcype) **C** in a similar manner.