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Doctoral Dissertation

Studies on Halogen Exchange of Transition-metal Complexes and Intramolecular Acylfluorination of Alkynes Utilizing Acid Halides

Atsushi Sanagawa

January 2015

Graduate School of Engineering
Osaka University
Doctoral Dissertation

Studies on Halogen Exchange of Transition-metal Complexes and Intramolecular Acylfluorination of Alkynes Utilizing Acid Halides

(酸ハライド類を用いる遷移金属錯体のハロゲン交換反応およびアルキニン類の分子内アシルフルオロ化反応に関する研究)

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Preface

The study described in this thesis has been carried out (2009-2015) under the direction of Professor Nobuaki Kambe and Associate Professor Hitoshi Kuniyasu at Department of Applied Chemistry, Graduate School of Engineering, Osaka University. The objective of this thesis is concerned with studies on the halogen-exchange reaction between various transition-metal complexes and acid halides and Lewis acid catalyzed intramolecular additions of acid fluorides to alkynes.
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General Introduction

Transition-metal catalyzed reactions consist of several elementary reactions such as oxidative additions, transmetalation, insertion, \(\beta\)-elimination, and reductive elimination (Scheme 1). The understanding of these processes is crucial to develop new reactions.

![Scheme 1](image_url)

Scheme 1. Transition-metal Catalyzed Reactions Trigged by Oxidative Addition

Among them, oxidative additions of acid halides (RC(O)-X; X = halogen) to low-valent transition metals(M) affording acyl complexes (RC(O)-M-X) are quite fundamental (Scheme 2).\(^1\) A number of catalytic reactions\(^2\)-\(^5\) involving such reactions as a key step have been intensively developed. The cross-coupling reactions of acid chloride with organometal reagents,\(^2\) reduction,\(^3\) Heck type reactions\(^5\) and additions to unsaturated compounds\(^6\) are among remarkable examples using acid halides (Scheme 3).

![Scheme 2](image_url)

Scheme 2. Oxidative Addition of Acid Halides
Thioesters (RC(O)-X; X = SR’), acid halides deliverives, are readily accessible molecules, stable under air and useful building blocks. In organometallic chemistry, the reactivity of thioesters toward transition metal complexes (oxidative addition of carbonyl-sulfur bonds of thioesters to transition metal complexes) lies in between esters and acid chlorides. Thioesters have been extensively employed as substrates in transition-metal catalyzed reactions.7 Our research group has studied on stoichiometric reactions using thioesters as substrates and has developed its application to the catalytic systems utilizing of reactivity differences between acid halides and thioesters.8

Because acid bromides and acid iodides which show higher reactivity than chloride are unstable and difficult to handle, acid chlorides are often used as reaction substrates in the above-mentioned reactions. The reaction utilizing fluorine atom of acid fluorides for organic synthesis is little known.9 The author thought that little noticed acid halides may have the hidden potential as substrates for stoichiometric and catalytic reactions.

The author launched a study on novel transformations of transition-metal complexes and catalytic reaction utilizing characteristic reactivity of acid halides. The present thesis consists of the halogen-exchange reactions of various transition-metal complexes with acid halides and Lewis acid catalyzed intramolecular addition reaction of acid fluorides to alkynes.

In chapter 1, the efficient halogen exchange reactions between palladium/platinum complexes and acid halides are discrbed.

\[
\begin{align*}
\text{Ph}^{-}X^{-} + \text{Ph}^{-}M^{-}X' & \rightleftharpoons \text{Ph}^{-}X' + \text{Ph}^{-}M^{-}X' \\
X, X' &= \text{Cl, Br, I} \quad M = \text{Pd, Pt}
\end{align*}
\]
In chapter 2, the halogen exchange reactions between aurous complexes and acid halides are described.

\[
\begin{align*}
\text{MeCO}_X + \text{Ph}_3\text{PAuCl} & \rightarrow \text{MeCO}_\text{Cl} + \text{Ph}_3\text{PAuX} \\
X &= \text{Br, I}
\end{align*}
\]

In chapter 3, the halogen exchange reactions between ruthenium complexes and acid halides are described.

\[
\begin{align*}
\text{MeCO}_X + \text{Ph}_3\text{P}^+\text{Ru}_{\text{Cl}}\text{PPh}_3 & \rightarrow \text{MeCO}_\text{Cl} + \text{Ph}_3\text{P}^+\text{Ru}_X\text{PPh}_3
\end{align*}
\]

In chapter 4, Lewis acid catalyzed intramolecular acyl fluorination of alkynes is described.

\[
\text{MeCO}_X + \text{Ph} \rightarrow \text{MeCO}_F + \text{Ph}
\]
References and Notes


1-1 Introduction

Ligand-exchange reactions are fundamental transformations in organometallic chemistry, and their representative reaction types are shown in Scheme 1.\(^1\) Eq 1 represents an exchange between neutral compounds \(L^1\) and \(L^2\), a process involved in a number of transition-metal-catalyzed reactions for incorporating organic substrates into the metal catalyst and liberating products from the coordination site. Exchange of \(M^1–X\) (\(X\): anionic element or functionality) with a different low-valent metal complex (\(M^2\)) is known as redox transmetalation (Eq 2).\(^2\) Transmetalation that involves an exchange between \(M^1–X\) (\(M^1\): transition metal) and \(M^2–R\) (\(M^2\): metals such as Mg, Zn, and B; \(R\): carbon or heteroatom functional group) is also widely employed in many catalytic reactions such as cross-coupling (Eq 3).\(^3\) For reactions represented by Eq 4, Tanaka and coworkers briefly reported the ligand-exchange reaction of PhTe of trans-Pd(Ph)(TePh)(PEt\(_3\))\(_2\) with I of PhI to afford trans-Pd(I)(Ph)(PEt\(_3\))\(_2\).\(^4a\) However, the general significance of ligand-exchange reactions between \(M–X\) and \(R–X’\) has not been completely recognized.\(^4\)

\[
\begin{align*}
\text{Scheme 1. Representative Reaction Types of Ligand-Exchange Reactions (L: neutral ligand; X, X’: halogen or pseudo halogen)}

\text{1) } & M-L^1 + L^2 & \rightleftharpoons & M-L^2 + L^1 & (1) \\
\text{2) } & M^1-X + M^2 & \rightleftharpoons & M^1 + M^2-X & (2) \\
\text{3) } & M^1-X + M^2-R & \rightleftharpoons & M^1-R + M^2-X & (3) \\
\text{4) } & M-X + R-X' & \rightleftharpoons & M-X' + R-X & (4)
\end{align*}
\]

Herein, we wish to demonstrate the following: (1) the utility of such ligand-exchange reactions for determining the relative \(\Delta G_s\) of the oxidative addition of acid halides RC(O)X (1, \(X = \text{Cl}\); 2, \(X = \text{Br}\); 3, \(X = \text{I}\)) to \(M(PPh_3)_2\)\(Ln\) (4, \(M = \text{Pt}\); 5, \(M = \text{Pd}\)) producing trans-\(M(X)[C(O)R](PPh_3)_2\) (6, \(M = \text{Pt}, X = \text{Cl}\); 7, \(M = \text{Pt}, X = \text{Br}\); 8, \(M = \text{Pt}, X = \text{I}\); 9, \(M = \text{Pd}, X = \text{Cl}\); 10, \(M = \text{Pd}, X = \text{Br}\); 11, \(M = \text{Pd}, X = \text{I}\)) and \(n\)L (Eq 5); (2) its reaction mechanism by density functional theory (DFT) method; and (3) synthetic application of the method for the
conversion of M-X bonds into M-X’ bonds with heavier halogens.

\[
\begin{align*}
1, X = \text{Cl} & & 4, M = \text{Pt} \\
2, X = \text{Br} & & 5, M = \text{Pd} \\
3, X = \text{I} & & 6, M = \text{Pt}, X = \text{Cl} \\
a, R = \text{Ph} & & 7, M = \text{Pt}, X = \text{Br} \\
b, R = \text{C}_6\text{H}_4\text{Me-}p & & 8, M = \text{Pt}, X = \text{I} \\
c, R = \text{Me} & & 9, M = \text{Pd}, X = \text{Cl} \\
d, R = \text{C}_6\text{H}_4\text{Me-p} & & 10, M = \text{Pd}, X = \text{Br} \\
e, R = \text{Me} & & 11, M = \text{Pd}, X = \text{I}
\end{align*}
\]

1-2 Results and Discussion

During the course of our studies to clarify the reactivity of C-X bonds of RC(O)-X toward M(0) (M = Pt and Pd),\(^5\)\(^8\) we found that the type-4 ligand-exchange reaction between trans-M(X)(C(O)R)(PPh\(_3\))\(_2\) and RC(O)X’ occurred successfully. For instance, the solution of trans-Pt(Cl)(C(O)Ph)(PPh\(_3\))\(_2\) (trans-6a) (0.02 mmol, \(\delta 20.4\), \(J_{\text{Pt-P}} = 3360\) Hz by \(^{31}\)P NMR spectrum) and PhC(O)Br (2a, 0.02 mmol) in benzene-\(d_6\) (0.7 mL) at 35 \(^\circ\)C produced an equilibrium mixture of trans-6a + 2a (system A) and trans-Pt(Br)(C(O)Ph)(PPh\(_3\))\(_2\) (trans-7a) (\(\delta 19.8, J_{\text{Pt-P}} = 3340\) Hz) + PhC(O)Cl (1a) (system B) within 24 h (Eq 6); in this reaction, Cl of trans-6a was exchanged with Br of 2a. Neither intermediate nor cis-isomer was detected during the reaction.

\[
\begin{align*}
\text{(A)} & & \Delta G_{\text{Exc-Br-Cl}} = -15.2 \pm 0.7 \text{ kJ/mol} \\
\text{(B)}
\end{align*}
\]

**Scheme 2.** \(\Delta G_{\text{Exc-Br-Cl}}\) Calculation by the Halogen-Exchange Reaction

By applying the equilibrium constants \(K\) to the equation \(\Delta G = -RT\ln K\), the energy gap between A and B (\(\Delta G_{\text{Exc-Br-Cl}}\)) was calculated as \(-15.2 \pm 0.7\) kJ/mol (Scheme 2).\(^9\) Considering a reaction system consisting of one equivalent of PhC(O)Cl (1a), PhC(O)Br (2a), and Pt(PPh\(_3\))\(_2\)L\(_6\) (4) (Scheme 3, C), the oxidative addition of 1a to 4 gives D (trans-6a + 2a + nL = A + nL) with free energy change \(\Delta G_{\text{OA-Cl}}\), whereas the reaction of 2a with 4 gives E (trans-7a + 1a + nL = B + nL), accompanied by \(\Delta G_{\text{OA-Br}}\). Accordingly, \(\Delta G_{\text{Exc-Br-Cl}}\) obtained from Eq 6 is
equal to the free energy gap between $\Delta G_{OA-Br}$ and $\Delta G_{OA-Cl}$ ($\Delta G_{\text{Exc-Br-Cl}} = \Delta G_{OA-Br-Cl}$).\textsuperscript{10,11}

![Diagram](image)

**Scheme 3.** Evaluation of $\Delta \Delta G_{OA-Br-Cl}$

Similarly, the solution of *trans*-7a and PhC(O)I (3a) produced an equilibrium mixture of *trans*-7a + 3a and *trans*-Pt(I)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-8a) + PhC(O)Br (2a); therefore, from $\Delta G_{\text{Exc-I-Br}}$ of this ligand exchange reaction, it can be concluded that the addition of 3a to Pt(PPh\textsubscript{3})\textsubscript{2}L\textsubscript{0} (4) producing trans-8a and nL is $-10.9 \pm 0.4$ kJ/mol ($\Delta \Delta G_{OA-I-Br}$) more favorable than that of 2a to 4, yielding *trans*-7a and nL. A similar treatment of *trans*-Pt(Cl)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-6a) with PhC(O)I (3a) gave both *trans*-Pt(I)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-8a) and PhC(O)Cl (1a) exclusively within 25 min at 20 °C. Although $\Delta \Delta G_{OA-I-Cl}$ cannot be directly calculated from this experimental data, it is quantitatively evaluated by assuming a system comprising one equivalent of 1a, 2a, 3a, and 4 (F (C + 3a)). Consider the addition reactions of 1a, 2a, and 3a to 4 produce G (trans-6a + 2a + 3a + nL = D + 3a), H (trans-7a + 1a + 3a + nL = E + 3a), and I (trans-8a + 1a + 2a + nL) accompanied by $\Delta G_{OA-CI}$, $\Delta G_{OA-Br}$, and $\Delta G_{OA-I}$, respectively. The value of $\Delta \Delta G_{OA-I-Cl}$ is clearly the gap between G and I, i.e., the sum of $\Delta \Delta G_{OA-Br-Cl}$ and $\Delta \Delta G_{OA-I-Br}$ (-26.1 ± 0.8 kJ/mol).\textsuperscript{12,13}

Similarly, the reactions between the corresponding palladium complexes *trans*-Pd(Cl)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-9a) and PhC(O)Br (2a) afforded the equilibrium mixture of *trans*-9a + 2a and *trans*-Pd(Br)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-10a) + 1a within 60 min at 20 °C: the value of $\Delta \Delta G_{OA-Br-Cl}$ was $-14.6 \pm 0.1$ kJ/mol. From the reaction of *trans*-10a with 3a producing an equilibrium mixture of *trans*-Pd(Br)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-10a) + 3a and *trans*-Pd(I)[C(O)Ph](PPh\textsubscript{3})\textsubscript{2} (trans-11a) + 2a, $\Delta \Delta G_{OA-I-Br}$ was determined to be $-6.9 \pm 0.1$ kJ/mol. Accordingly, $\Delta \Delta G_{OA-I-Cl}$ was calculated to be $-21.5 \pm 0.2$ kJ/mol. These results are summarized in Tables 1.

Next, $\Delta \Delta G$ values were theoretically evaluated using M[C(O)Ph](PPh\textsubscript{3})\textsubscript{2}X as model compounds by DFT calculation with the TPSS functional (Table 1).\textsuperscript{14,15} $\Delta \Delta G_{OA-BR-Cl}$ (t: theoretical), $\Delta \Delta G_{OA-I-Br}$, and $\Delta \Delta G_{OA-I-Cl}$ were $-17.3$, $-11.5$, and $-28.9$ kJ/mol, respectively (the left column of Table 1). The data with the corresponding palladium complexes are also summarized in the right column of Table 2. $\Delta \Delta G_{OA-BR-Cl}$, $\Delta \Delta G_{OA-I-Br}$, and $\Delta \Delta G_{OA-I-Cl}$ were $-20.5$, $-13.0$, and $-33.5$ kJ/mol, respectively. These results demonstrate that $\Delta \Delta G$ obtained
from the experiment are relatively consistent with those of the theoretical calculation, indicating the reliability of the $\Delta \Delta G$ calculation.

Table 1. $\Delta \Delta G_{OA-X'-X}$ by Experiment and $\Delta \Delta G_{OA-X'-X-t}$ by DFT Calculation$^{[a][b]}$ (kJmol$^{-1}$)

<table>
<thead>
<tr>
<th>$X'$</th>
<th>$X$</th>
<th>Exptl $\Delta \Delta G_{OA-X'-X}$</th>
<th>Theor $\Delta \Delta G_{OA-X'-X-t}$</th>
<th>Exptl $\Delta \Delta G_{OA-X'-X}$</th>
<th>Theor $\Delta \Delta G_{OA-X'-X-t}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br</td>
<td>Cl</td>
<td>$-15.2 \pm 0.7$</td>
<td>$-17.3$</td>
<td>$-14.6 \pm 0.1$</td>
<td>$-20.5$</td>
</tr>
<tr>
<td>I</td>
<td>Br</td>
<td>$-10.9 \pm 0.4$</td>
<td>$-11.5$</td>
<td>$-6.9 \pm 0.1$</td>
<td>$-13.0$</td>
</tr>
<tr>
<td>I</td>
<td>Cl</td>
<td>$-26.1 \pm 0.8$</td>
<td>$-28.9$</td>
<td>$-21.5 \pm 0.2$</td>
<td>$-33.5$</td>
</tr>
</tbody>
</table>

[a]Model systems; $M[C(O)Ph](PH_3)_2X + PhC(O)X' \rightarrow M[C(O)Ph](PH_3)_2X' + PhC(O)X$

[b]TPSS functional was employed for the calculation of $\Delta \Delta G$ values with the basis set: 6-31G(d,p) for H, C, and O atoms; Def2-TZVP for P, Cl and Br atoms; and Def2-TZVP with the effective core potential for Pt, Pd and I atoms.

To gain insight into the mechanism of the present halogen-exchange, the reaction of trans-Pt(Cl)[C(O)Ph](PPh$_3$)$_2$ (trans-6a) with $p$-MeC$_6$H$_4$C(O)Br (2b) was examined (Eq 7). The reaction selectively afforded a mixture of trans-6a and trans-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (trans-7a) in a ratio of 2:98. Neither trans-Pt(Cl)[C(O)C$_6$H$_4$Me-$p$](PPh$_3$)$_2$ (trans-6b) nor trans-Pt(Br)[C(O)C$_6$H$_4$Me-$p$](PPh$_3$)$_2$ (trans-7b) was observed, suggesting that the reaction of trans-Pt(Cl)[C(O)Ph](PPh$_3$)$_2$ (trans-6a-1) with PhC(O)Br (2a-1) provides trans-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (trans-7a-1) and PhC(O)Cl (1a-2).

\[
\text{trans-6a} + 35 \degree C \rightarrow \text{trans-6a} + \text{trans-7a} \quad 2:98
\]

\[
\begin{align*}
\text{trans-6a} & \quad \text{2b} \\
\text{trans-6b} & \quad \text{nd} \\
\text{trans-7a} & \quad \text{nd} \\
\end{align*}
\]

The mechanism involving reductive elimination of PhC(O)Cl (1a) from trans-6a to give coordinatively unsaturated Pt(PPh$_3$)$_2$, followed by the oxidative addition of PhC(O)Br (2a), to form trans-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (trans-7a) is ruled out. $\Delta \Delta G$ of the oxidative addition of acid halides to Pt(PPh$_3$)$_2$L$_n$ (4) can be determined from the present ligand-exchange reaction; however, the process itself is not involved in the transformation. This fact also demonstrated that the formation Pt(IV) intermediates can be ruled out. Moreover, to obtain information about the effect of the polarity of the solvent, the reaction of trans-6a with 2a in CD$_2$Cl$_2$ was monitored by $^{31}$P NMR spectrum, and reaction rate was compared with that of benzene-$d_6$. As
a result, there was no remarkable difference observed in reaction rate. In addition, the rate of the ligand-exchange reaction was hardly influenced by the addition of free PPh₃, TEMPO, or galvinoxyl, which suggests that participation of both a cationic complex \{Pt[\text{C}(\text{O})\text{Ph}](\text{PPh}_3)_3\}^+X^- and radical species were improbable. To obtain additional information about the reaction mechanism, the activation parameters of the reaction of trans-6a (0.01 mmol) with an excess of 2a (0.20 mmol) to afford trans-7a and 1a were calculated by measuring the temperature dependence of reaction rate (−10 ~ 20 °C). The values of Δ\(H^\ddagger\) and Δ\(S^\ddagger\) were successfully measured to be 44 ± 3 and −148 ± 9 J/Kmol, respectively.

Next, the mechanism of the \(\sigma\)-bond metathesis shown in Scheme 4 were theoretically examined with the M06 functional. A transition state TS1 was successfully located and the energy diagram of the reaction coordinate and two different views of the structure of TS1 are shown in Figures 1 and 2, respectively.

Scheme 5. Possible \(\sigma\)-Bond Metathesis Mechanisms

TS1 is 48.1 kJ/mol energetically higher than the starting reaction system (trans-6a-1 + 2a-2). The value is relatively consistent with Δ\(H^\ddagger\) obtained from the experimental data. Moreover, the value of Δ\(S^\ddagger\) calculated theoretically was −137.9 J/Kmol, which is also consistent with the experimental data. The selected bond distances of the optimized structures of reactants, transition state, and products involved in the reaction mechanism are summarized in Figure 3. When the Pt-Cl bond of trans-6a-1 (2.55 Å) is compared with that of TS1 (2.97 Å), the bond is stretched by 0.42 Å. On the other hand, the C-Br bond elongation difference between 2a-2 (2.01 Å) and TS1 (2.13 Å) is only 0.12 Å. The bond length difference of C-Cl between TS1 (2.38 Å) and 1a-2 (1.84 Å) is 0.54 Å, whereas the Pt-Br bond in TS1 (2.82 Å) shrinks by 0.19 Å with respect to that in trans-7a-1a (2.63 Å). Therefore, both Pt-Cl and C-Cl bonds undergo more dynamic bond changes than C-Br and Pt-Br bonds. In other words, the Cl atom takes a more roundabout route than the Br atom during the course of \(\sigma\)-bond metathesis. The C=O bond length of C² of TS1 is 1.185 Å, which is barely different from that of free 2a-2 and 1a-2 (1.190 Å).
Figure 1. Reaction coordinate of pentacoordinated σ-bond metathesis from *trans*-6a-1

Figure 2. Structure of TS1 of the Pt-complex via pentacoordinated σ-bond metathesis from *trans*-6a-1 (two different views).

Figure 3. Selected bond distances (Å) of the optimized structures of reactants, TS1 and products.
The transition state of the pentacoordinated σ-bond metathesis was also located for the reaction of the corresponding palladium complex, *trans*-9a-1, with PhC(O)Br (2a-2). The reaction coordinate and structure of the transition state TS2 are shown in Figures 4 and 5, respectively. Energy of TS2 is only 15.5 kJ/mol higher than that of the reactant (*trans*-9a-1 + 2a-2), which is consistent with the fact that the reaction of *trans*-9a with 2a occurred faster than that using the corresponding platinum complex *trans*-6a.

**Figure 4.** Reaction coordinate of pentacoordinated σ-bond metathesis from *trans*-9a-1.

**Figure 5.** Structure of TS2 of the Pd-complex formed from *trans*-9a-1 via pentacoordinated σ-bond metathesis (two different views).
When the bond of Pd-Cl of trans-9a-1 is compared with that of TS2 (2.49 Å vs. 3.25 Å), the gap is 0.76 Å. The difference in the bond lengths of C-Br between 2a-2 (2.01 Å) and TS3 (2.30 Å) is 0.29 Å. On the other hand, the difference in the bond lengths of C-Cl between TS3 (2.26 Å) and 1a-2 (1.84 Å) and that in the bond length of Pd-Br between TS2 (2.68 Å) and trans-10a-1 (2.58 Å) are 0.42 and 0.10 Å, respectively. Again, these results indicated that the Cl atom takes a more circuitous route than the Br atom during σ-bond metathesis. On the basis of the above mentioned discussions, we concluded that pentacoordinated σ-bond metathesis of trans-M(X)[C(O)R](PPh₃)₂ and RC(O)X’ is the most probable mechanism for the present halogen-exchange reaction.

Because it became evident that only halogen atoms were exchanged, the utility of this transformation as a halogen-exchange prototype was examined as follows: after the reaction of 1.0 mmol cis-[Pt(Cl)₂(PPh₃)₂] (12) with 4.0-mmol MeC(O)(Br) (2c) in CH₂Cl₂ (50 mL) at 20 °C for 30 min, the solvent, excess 2c (b.p. 75 ºC–77 ºC), and byproduct of MeC(O)(Cl) (1c) (b.p. 52 ºC) were removed by subjecting the reaction mixture under reduced pressure to produce the analytically pure cis-[Pt(Br)₂(PPh₃)₂] quantitatively (Eq 8). The removal of salt by filtration, washing with water, drying with desiccant, and recrystallization, which are generally required by the conventional Cl-to-Br exchange reaction with a typical element metal salt such as LiBr and NaBr, were not required. Moreover, the corresponding iodide was isolated similarly by the treatment of 12 with CH₃C(O)I (3c, b.p. 108 ºC) and subsequent evaporation. Similarly, the reaction of trans-[Pd(Cl)₂(PPh₃)₂] (13) with 2c and 3c afforded trans-[Pd(Br)₂(PPh₃)₂] and trans-[Pd(I)₂(PPh₃)₂], respectively (Eq 9). This methodology of the halogen-exchange reaction was also applicable to complexes with alkyl phosphine or nickel complexes. The conversions of the trans-[Pd(Cl)₂(PEt₃)₂] (14) and [Ni(Cl)₂(dppe)] (15) into trans-[Pd(X)₂(PEt₃)₂] and [Ni(X)₂(dppe)] (X = Br and I) were facilely achieved (Eq 10 and...
The significance of the present study is summarized as follows: (1) the reactions of \( \text{trans-M}(X)[\text{C(O)R}](\text{PPh}_3)_2 \) with \( \text{RC(O)}X' \) produced clean equilibrium mixtures of \( \text{trans-M}(X)[\text{C(O)R}](\text{PPh}_3)_2/\text{RC(O)}X' \) and \( \text{trans-M}(X')[\text{C(O)R}](\text{PPh}_3)_2/\text{RC(O)}X \); (2) \( \Delta G \) values were equal to the relative \( \Delta G_s \) of the oxidative additions of \( \text{RC(O)}X/\text{RC(O)}X' \) to \( \text{M(PP}_3)_2\text{Ln} \), which was clearly supported by DFT calculation; (3) both experimental and computational studies substantiated that the reaction occurred via pentacoordinated \( \sigma \)-bond metathesis, in which significant behavioral disparity was suggested between Cl and Br atoms; and (4) the ligand-exchange reaction can be utilized as a simple prototype to convert chloro ligands into heavier halogen ligands of nickel triad complex.

1-4 Experimental Section

General Comments

The \( ^{31}\text{P} \) spectra in benzene-\( d_6 \) were recorded with a JEOL JNM AL400 and ECS400 (160 MHz) spectrometers, the chemical shifts were recorded relative to 85% \( \text{H}_3\text{PO}_4 \) (aq) as an external standard, and \( \text{S=Ps(C}_6\text{H}_4\text{OMe-p})_3 \) was used as an internal standard to calculate the yields of products. The sensitivities of platinum and palladium complexes to the internal standard were measured individually. Benzoyl chloride (1a), benzoyl bromide (2a), \( p\)-\text{MeC}_6\text{H}_4\text{C(O)Cl} \) (1c), and \( \text{MeC(O)Cl} \) (1d) were commercially obtained. \( p\)-\text{MeC}_6\text{H}_4\text{C(O)Br} \) (2b) and \( p\)-\text{MeC}_6\text{H}_4\text{C(O)I} \) (3b) were synthesized by the reaction of 1c with \( \text{Me}_3\text{SiBr} \) and \( \text{Me}_3\text{SiI} \) (Synthesis, 1981, 216), respectively. Other acid bromides and iodides were obtained similarly. Benzene-\( d_6 \) was purified by distillation from sodium benzophenone ketyl before use. The authentic samples of \( \text{trans-M}(X)[\text{C(O)R}](\text{PPh}_3)_2 \) (6, \( M = \text{Pt}, X = \text{Cl}; 7, M = \text{Pt}, X = \text{Br}; 8, M = \text{Pt}, X = I; 9, M = \text{Pd}, X = \text{Cl}; 10, M = \text{Pd}, X = \text{Br}; 11, M = \text{Pd}, X = I) \) were prepared by the
reaction of Pt(PPh\(_3\))\(_2\)(C\(_2\)H\(_4\)) or Pd(PPh\(_3\))\(_4\) with the corresponding acid halides, respectively. Registry No. of trans-6a: 018421-48-2; trans-7a: 57665-38-0; trans-8a: 60751-00-0.

trans-6a: \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 20.4 \((J_{Pt-P} = 3360 \text{ Hz})\).

trans-7a: \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 19.8 \((J_{Pt-P} = 3340 \text{ Hz})\).

trans-8a: \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 17.5 \((J_{Pt-P} = 3300 \text{ Hz})\).

**The Synthesis of trans-Pd(Cl)[C(O)Ph](PPh\(_3\))\(_2\) (9a)**

Into a reaction vessel were added Pd(PPh\(_3\))\(_4\) (577 mg, 0.5 mmol), toluene (25 mL) and 1a (77 mg, 0.55 mmol) at 25 °C in a glove box. After the reaction mixture was stirred for 90 min, 25 mL of dry Et\(_2\)O was added into the solution and the resultant mixture was cooled at -25 °C in a refrigerator. Then the precipitate was filtrated off and dried under vacuum to give the desired trans-9a as a pale yellow solid (341 mg, 77%).

trans-9a: mp 180 °C (dec.) (a pale yellow solid); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 6.74 (t, \(J = 7.3 \text{ Hz}, 2 \text{ H}\)), 6.83 (t, \(J = 7.3 \text{ Hz}, 1 \text{ H}\)), 6.93-6.95 (m, 18 H), 7.89-7.99 (m, 14 H); IR (KBr) 3053, 1638, 1480, 1434, 1182, 1148, 1094, 869, 778, 744; \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 19.22 (s); Anal. Calcd for C\(_{43}\)H\(_{35}\)ClOP\(_2\)Pd: C, 66.94; H, 4.57. Found: C, 67.04; H, 4.60.

The trans-Pd(Br)[C(O)Ph](PPh\(_3\))\(_2\) (trans-10a) and trans-Pd(I)[C(O)Ph](PPh\(_3\))\(_2\) (trans-11a) were also prepared by similar procedures.

trans-10a (82%): mp 190 °C (dec.) (a pale yellow solid); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 6.76 (t, \(J = 7.3 \text{ Hz}, 2 \text{ H}\)), 6.84 (t, \(J = 7.2 \text{ Hz}, 1 \text{ H}\)), 6.93-6.95 (m, 18 H), 7.89-7.99 (m, 14 H); IR (KBr) 3053, 1650, 1481, 1435, 1183, 1149, 871, 743, 691, 633 cm\(^{-1}\); \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 19.22 (s); Anal. Calcd for C\(_{43}\)H\(_{35}\)BrOP\(_2\)Pd: C, 63.29; H, 4.32. Found: C, 63.32; H, 4.22.

trans-11a (79%): 185°C (dec.) (a pale yellow solid) \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 6.75-6.87 (m, 3 H), 6.93-6.95 (m, 18 H), 7.92-7.97 (m, 14 H); IR (KBr) 3054, 1636, 1481, 1435, 1183, 1149, 871, 743, 691, 633 cm\(^{-1}\); \(^{31}\)P NMR (161 MHz, C\(_6\)D\(_6\)) \(\delta\) 19.18 (s); Anal. Calcd for C\(_{43}\)H\(_{35}\)IOP\(_2\)Pd: C, 59.84; H, 4.09. Found: C, 60.12; H, 4.00.

All the reaction samples described below were prepared in a glove box and hydrolysis was strictly prevented.

**Halogen Exchange Reaction between Cl of trans-Pt(Cl)[C(O)Ph](PPh\(_3\))\(_2\) (trans-6a) and Br of PhC(O)Br (2a)**

Into a dry Pyrex NMR tube were added S=P(C\(_6\)H\(_4\)OMe-p)\(_3\) (1.9 mg, 0.0050 mmol as an internal standard), trans-6a (17.1 mg, 0.0199 mmol), and benzene-\(d_6\) (0.5 mL). After the
sensitivity of *trans*-6a to the internal standard was measured by $^{31}$NMR spectrum, PhC(O)Br (2a, 2.2 mg, 0.0200 mmol) was added. Then, the reaction at 35 °C was monitored by $^{31}$P and $^1$H NMR spectroscopies. The gradual formation of *trans*-7a was observed. Within 24 h, the mixture reached the equilibrium state between *trans*-6a + 2a and *trans*-7a + 1a. Neither cis-6a nor cis-7a was detected during the course of the reaction. The equilibrium constant $K = [1a][\text{trans}-7a]/[2a][\text{trans}-6a]$ was calculated to be $2.5 \times 10^2$. By applying this equilibrium constant to an equation $\Delta G = -RT\ln K$, $\Delta G_{\text{Exc-Br-Cl}}$ was calculated to be $-14.6$ kJ/mol. From the data obtained from several similar experiments as well as starting from *trans*-7a and 1a, the average $\Delta G_{\text{Exc-Br-Cl}}$ was calculated to be $-15.2 \pm 0.7$ kJ/mol. The standard error, which was calculated by using statistical method equipped in Excel program, was employed for expressing the margin of error.

The treatments of 1a, 2a, and Pt(PPh$_3$)$_2$(C$_2$H$_4$) in benzene-$d_6$ also produced a similar equilibrium mixtures with the virtually identical $K$ value.

The reaction of *trans*-7a (18.0 mg, 0.0199 mmol) with PhC(O)I (3a, 5.2 mg, 0.022 mmol) also afforded an equilibrium mixture between *trans*-7a + 3a and *trans*-8a + 2a. From the equilibrium constants obtained under several experiments, $\Delta G_{\text{Exc-I-Br}}$ was calculated to be $-10.9 \pm 0.4$ kJ/mol. On the other hand, the reaction of *trans*-6a with 3a under similar conditions quantitatively produced *trans*-8a and 1a. The $\Delta G_{\text{Exc-I-Cl}}$ value was calculated to be $-26.1 \pm 0.8$ kJ/mol as a sum of $\Delta G_{\text{Exc-Br-Cl}}$ and $\Delta G_{\text{Exc-I-Br}}$ using the low of error propagation.

**Halogen Exchange Reaction between Cl of *trans*-Pd(Cl)[C(O)Ph](PPh$_3$)$_2$ (trans-9a) and Br of PhC(O)Br (2a)**

Into a dry Pyrex NMR tube were added S=Ph(C$_3$H$_4$OMe-p)$_3$ (1.9 mg, as an internal standard), *trans*-9a (7.7 mg, 0.010 mmol), and benzene-$d_6$ (0.5 mL). After the sensitivity of *trans*-9a to the internal standard was measured by $^{31}$NMR spectrum, PhC(O)Br (2a, 2.2 mg, 0.0200 mmol) was added. Then, the reaction at 20 °C was monitored by $^{31}$P and $^1$H NMR spectroscopies. It was found that the mixture reached the equilibrium state between *trans*-9a + 2a and *trans*-10a + 1a within 60 min. By applying the equilibrium constant to the equation $\Delta G = -RT\ln K$, the average $\Delta G_{\text{Exc-Br-Cl}}$ was calculated as $-14.6 \pm 0.1$ kJ/mol from similar five-time experiments. The treatment of 1a and 2a with Pd(PPh$_3$)$_4$ in benzene-$d_6$ also produced equilibrium mixtures with the virtually identical $K$ value.

The reaction of *trans*-10a with PhC(O)I (3a) also afforded an equilibrium mixture between *trans*-10a + 3a and *trans*-11a + 2a. From the equilibrium constant obtained from similar five-time measurements, the average $\Delta G_{\text{OA-Br-Cl}}$ was calculated to be $-6.9 \pm 0.1$ kJ/mol. On the other hand, the reaction of *trans*-9a with 3a under similar conditions quantitatively produced *trans*-11a and 1a quantitatively. The $\Delta G_{\text{Exc-I-Cl}}$ value was calculated to be $-21.5 \pm 0.2$ kJ/mol as a sum of $\Delta G_{\text{OA-Br-Cl}}$ and $\Delta G_{\text{Exc-I-Br}}$. 

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**Halogen Exchange Reaction between trans-6a and p-MeC₆H₄C(O)Br (2b)**

Into a dry Pyrex NMR tube were added trans-6a (8.4 mg, 0.0098 mmol), p-MeC₆H₄C(O)Br (2c, 2.4 mg, 0.012 mmol), S=P(C₆H₄OMe-p)₃ (1.2 mg, 0.0031 mmol) and benzene-d₆ (0.5 mL). The reaction at 35 °C was monitored by ³¹P and ¹H NMR spectroscopies. After 21 h, a mixture of trans-6a and trans-7a was produced in a ratio of 2:98. However, neither Pt(Cl)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-6b) nor Pt(Br)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-7b) was detected. On the other hand, the reaction of Pt(Cl)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-6b) with PhC(O)Br (2a) produced trans-Pt(Br)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-7b). However, neither trans-6a nor trans-7a was detected.

trans-6c: ³¹P NMR (161 MHz, C₆D₆) δ 18.9 (J_Pt-P = 3408 Hz) (data collected by the reaction of 1c with Pt(PPh₃)₂(C₂H₄))

trans-7c: ³¹P NMR (161 MHz, C₆D₆) δ 18.2 (J_Pt-P = 3387 Hz) (data collected by the reaction of 2c with Pt(PPh₃)₂(C₂H₄) (4a))

Similarly, the reaction of trans-Pd(Cl)(C(O)Ph)(PPh₃)₂ (trans-9a) with 2b selectively produced trans-Pd(Br)(C(O)Ph)(PPh₃)₂ (trans-10a). Neither formation of trans-Pd(Cl)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-9b) nor trans-Pd(Br)(C(O)C₆H₄Me-p)(PPh₃)₂ (trans-10c) was confirmed.

trans-9c: ³¹P NMR (161 MHz, C₆D₆) δ 19.3 (data collected by the reaction of 1b with Pd(PPh₃)₄)

trans-10c: ³¹P NMR (161 MHz, C₆D₆) δ 19.6 (data collected by the reaction of 2b with Pd(PPh₃)₄)

**Halogen Exchange Reaction in the Presence of Free PPh₃**

Into a dry Pyrex NMR tube were added trans-6a (8.6 mg, 0.010 mmol), PhC(O)Br (2a, 2.2 mg, 0.0200 mmol), PPh₃ (0.3 mg, 10 mol%), S=P(C₆H₄OMe-p)₃ (1.9 mg, 0.0050 mmol) and benzene-d₆ (0.5 mL). The reaction at 35 °C was monitored by ³¹P and ¹H NMR spectroscopies. However, the reaction rate was not affected by the addition of PPh₃. The reaction of trans-6a with 2a performed in CD₂Cl₂ also took place with a similar reaction rate to the reaction carried out in C₆D₆.

**Halogen Exchange Reaction in the Presence of Radical Scavenger**

Into a dry Pyrex NMR tube were added trans-7a (9.1 mg, 0.010 mmol), PhC(O)I (3a, 2.2 mg, 0.0200 mmol), TEMPO (1.7 mg, 0.011 mmol), S=P(C₆H₄OMe-p)₃ (1.9 mg, 0.0050 mmol) and benzene-d₆ (0.5 mL) with the sample cooled by dry ice/i-PrOH bath. Then the reaction was monitored at -40 °C by ³¹P NMR spectroscopy. As a result, no significant effect on reaction rate was observed compared to the reaction performed without TEMPO. Similarly, the halogen
exchange reaction was not affected by the presence of 0.011 mmol of galvinoxyl.

**Activation Parameters**

Activation parameters of the transformation of trans-6a + 2a (10 equiv) to trans-7a + 1a were calculated by measuring the temperature dependence of the reaction rate in the range of -10 °C ~ 20 °C in toluene-d₈ according to the equation \( k = \left( \frac{k_B T}{h} \right) \exp\left[ -\left( \Delta H^\ddagger - T \Delta S^\ddagger \right) / (RT) \right] \). Reaction temperature and reaction rates (\( k_{\text{real}} \)) were as follows: 263 K, 1.92 x 10⁻⁴ L/molS; 3.93 x 10⁻⁴ L/molS; 283 K, 9.42 x 10⁻⁴ L/molS; 293 K, 15.83 x 10⁻⁴ L/molS. The values of \( \Delta H^\ddagger \) and \( \Delta S^\ddagger \) were successfully measured to be 44 ± 3 kJ/mol and -148 ± 9 J/Kmol, respectively.

**Halogen Exchange Reaction between Cl of trans-Pt(Cl)₂[(O)Ph]₂(PPh₃)₂ (trans-6a) and Br of MeC(O)Br (2d):**

Into a dry Pyrex NMR tube were added S=P(C₆H₄OMe-p)₃ (1.9 mg, as an internal standard), trans-6a (8.6 mg, 0.010 mmol), and benzene-d₆ (0.5 mL). After the sensitivity of trans-6a to the internal standard was measured by ³¹P NMR spectrum, MeC(O)Br (2d, 4.9 mg, 0.040 mmol) was added. Then, the reaction at 25 °C was monitored by ³¹P and ¹H NMR spectroscopies. It was found that trans-7a was produced quantitatively after 30 min.

**Synthetic Utility of the Present Halogen Exchange Reaction**

Into a 300 mL flask were added cis-Pt(Cl)₂(PPh₃)₂ (12, 701.9 mg, 1.0 mmol) and CH₂Cl₂ (50 mL). While the solution was stirred, 5.0 mmol of MeC(O)Br (2c) was added. After the solution was stirred for 30 min at 25 °C, CH₂Cl₂, 2c (b.p. 108 °C) and MeC(O)Cl (1c, b.p. 52 °C) were removed in vacuo to produce the analytically pure cis-Pt(Br)₂(PPh₃)₂ (870 mg) quantitatively. The corresponding iodide cis-Pt(I)₂(PPh₃)₂ was also isolated similarly with the treatment of 12 with CH₃C(O)I (3c). Similarly, the Cl atoms of trans-Pd(Cl)₂(PPh₃)₂, trans-Pd(Cl)₂(PET₃)₂, and Ni(Cl)(dppe)₂ were successfully converted into Br and I atoms by the treatment with 2c and 3c, respectively.

**Computational Details**

The DFT calculations of the equilibrium structures and the energetics of the intermediates and transition states were carried out by the GAUSSIAN09 suite of programs (Frisch, M. J. et al. GAUSSIAN09, Revision B.01; Gaussian, Inc.: Wallingford, CT, 2010). The following reaction model systems were employed for the theoretical calculations. The model systems was employed for the calculation of \( \Delta \Delta G \) values with the TPSS functional using the basis set: 6-31G(d,p) for H, C, and O atoms; Def2-TZVP for P, Cl and Br atoms; and Def2-TZVP with the effective core potential for Pt, Pd and I atoms. On the other hand, for the real systems of platinum and palladium complexes, the following basis set was employed with M06 functional:
6-31G(d,p) for Cl, Br, and P atoms as well as C and O atoms of the carbonyl groups; STO-6G for all the atoms in the phenyl groups (real system); [3s2p2d] with the relativistic effective core potential for Pt and Pd atoms. Geometry optimizations were performed without restricting the symmetry; all the calculations were performed under C1 symmetry. It was confirmed that all the intermediates are true local minima and all the transition states have only one imaginary frequency based on the vibrational analysis.

**Calculation of ΔGOA-X of Platinum Complexes with TPSS Functiona**

The Gibbs free energies (G) of the reactants and products in the reactions of PhC(O)X + Pt(PH3)2(C2H4) (4a') → trans-Pt(X)[C(O)Ph](PH3)2 + C2H4 (X = Cl, Br, and I) are shown in Table S1. The ΔGOA-X and ΔΔGOA-X-X' values obtained from the data are summarized in Table S2.

**Computational Model and Basis Set: TPSS**

Basis Set: H, C, and O: 6-31G (d,p); P and X (X = Cl and Br): Def2-TZVP; Pt and I: Def2-TZVP with effective core potential.

**Table S1.** Gibbs Free Energies (G) of the Reactants and Products in the Ligand Exchange Reaction (gas phase).

<table>
<thead>
<tr>
<th>Compound</th>
<th>G (a.u.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt(PH3)2(C2H4) (4a')</td>
<td>-884.3494</td>
</tr>
<tr>
<td>C2H4</td>
<td>-78.5760</td>
</tr>
<tr>
<td>trans-Pt(Cl)<a href="PH3">C(O)Ph</a>2 (6a')</td>
<td>-1611.0106</td>
</tr>
<tr>
<td>PhC(O)Cl (1a)</td>
<td>-805.2226</td>
</tr>
<tr>
<td>trans-Pt(Br)<a href="PH3">PhC(O)</a>2 (7a')</td>
<td>-3724.8480</td>
</tr>
<tr>
<td>PhC(O)Br (2a)</td>
<td>-2919.0534</td>
</tr>
<tr>
<td>trans-Pt(I)<a href="PH3">PhC(O)</a>2 (8a')</td>
<td>-1448.3853</td>
</tr>
<tr>
<td>PhC(O)I (3a)</td>
<td>-642.5863</td>
</tr>
</tbody>
</table>

**Table S2.** ΔGOA-X and ΔΔGXX' by Experiment in C6D6 and Theoretical Calculation in Gas Phase (kJ/mol).

<table>
<thead>
<tr>
<th></th>
<th>ΔGOA-Cl</th>
<th>ΔGOA-Br</th>
<th>ΔGOA-I</th>
<th>ΔΔGCl-Br</th>
<th>ΔΔGBr-I</th>
<th>ΔΔGCl-1</th>
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<tbody>
<tr>
<td>Expt.</td>
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<td>-</td>
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<td>-10.9±0.4</td>
<td>-26.1±0.8</td>
</tr>
<tr>
<td>Theory</td>
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<td>-55.66</td>
<td>-67.21</td>
<td>-17.3</td>
<td>-11.5</td>
<td>-28.9</td>
</tr>
</tbody>
</table>

1-2. Calculation of ΔGOA-X of Palladium Complexes with "middle model" with TPSS Functional

The Gibbs free energies (G) of the reactants and products in the reactions of PhC(O)X +
Pd(PH$_3$)$_2$(C$_2$H$_4$) (4a') $\rightarrow$ trans-Pd(X)[C(O)Ph](PH$_3$)$_2$ + C$_2$H$_4$  ($X$ = Cl, Br, and I) are shown in Table S3. The $\Delta G$ and $\Delta\Delta G$ values obtained from the data are summarized in Table S4.

Computational Model and Basis Set: TPSS
Basis Set: H, C, and O: 6-31G (d,p); P and X ($X$ = Cl and Br): Def2-TZVP; Pd and I: Def2-TZVP with effective core potential.

**Table S3.** Gibbs Free Energies (G) of the Reactants and Products in the Ligand Exchange Reaction (gas phase).

<table>
<thead>
<tr>
<th>Compound</th>
<th>G (a.u.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd(PH$_3$)$_2$(C$_2$H$_4$) (4a')</td>
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<tr>
<td>C$_2$H$_4$</td>
<td>-78.5679</td>
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<tr>
<td>trans-Pd(Cl)<a href="PH$_3$">C(O)Ph</a>$_2$ (9a')</td>
<td>-1619.4627</td>
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<tr>
<td>PhC(O)Cl (1a)</td>
<td>-805.1801</td>
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<td>trans-Pd(Br)<a href="PH$_3$">PhC(O)</a>$_2$ (10a')</td>
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<tr>
<td>PhC(O)Br (2a)</td>
<td>-2919.0239</td>
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<tr>
<td>trans-Pd(I)<a href="PH$_3$">PhC(O)</a>$_2$ (11a')</td>
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<td>PhC(O)I (3a)</td>
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</table>

**Table S4.** $\Delta G_{OA-X}$ and $\Delta\Delta G_{X-X'}$ by Experiment in C$_6$D$_6$ and Theoretical Calculation in Gas Phase (kJ/mol).

<table>
<thead>
<tr>
<th></th>
<th>$\Delta G_{OA-Cl}$</th>
<th>$\Delta G_{OA-Br}$</th>
<th>$\Delta G_{OA-I}$</th>
<th>$\Delta\Delta G_{Cl-Br}$</th>
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<tr>
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**Reaction Mechanisms through $\sigma$-Bond Metatheses**

**Table S5.** The Selected Bond Distances (Å) of Optimized Structures of Reactants, Transition State, and Products of the Reaction Mechanism through Pentacoordinated $\sigma$-Bond Metathesis from trans-6a-1 to trans-7a-1.

<table>
<thead>
<tr>
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<th>trans-6a-1</th>
<th>TS1</th>
<th>trans-7a-1</th>
<th>1a</th>
<th>2a</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_{Pt-Br}$</td>
<td>-</td>
<td>2.823</td>
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<tr>
<td>$R_{Pt-Cl}$</td>
<td>2.548</td>
<td>2.967</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$R_{C-Br}$</td>
<td>-</td>
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<td>-</td>
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<td>$R_{C-Cl}$</td>
<td>-</td>
<td>2.384</td>
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<tr>
<td>$R_{C-O}$</td>
<td>1.221</td>
<td>1.185</td>
<td>1.221</td>
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<td>1.190</td>
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Table S6. The Selected Interatomic Distances (Å) of the Reactants, Transition State, and Products of the Reaction Mechanism through Pentacoordinated σ-Bond Metathesis from Trans-9a.

<table>
<thead>
<tr>
<th>Compound</th>
<th>trans-9a</th>
<th>TS2</th>
<th>trans-10a</th>
<th>1a</th>
<th>2a</th>
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<tr>
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<td>(R_{PC-Br})</td>
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<td>(R_{PC-O})</td>
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Table S7. The Calculated Total Energies (\(E\)) and Energy Including Zero-point Energy Correction (\(E_{\text{zero}}\)) of the Reactants, Transition States, Intermediates, and Products.

<table>
<thead>
<tr>
<th>Compound</th>
<th>(E) (a.u.)</th>
<th>(E_{\text{zero}}) (a.u.)</th>
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<td>trans-6a-1</td>
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<td>-2991.055633</td>
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<td>2a-2</td>
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<td>-2915.630838</td>
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<td>1a-2</td>
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<tr>
<td>TS2</td>
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<tr>
<td>trans-10a-1</td>
<td>-5110.728794</td>
<td>-5110.040764</td>
</tr>
</tbody>
</table>

3-5 References and Notes


[9] The value was obtained as an average of ΔGs obtained from several experiments. The standard error was calculated by using a statistical method equipped in Excel program for expressing the margin of the error.


[12] Because the reactions of 1a, 2a, and 3a with Pt(PPh$_3$)$_2$(C$_2$H$_4$) (4a) and Pt(PPh$_3$)$_4$ (4b) both quantitatively produce trans-6a, trans-7a, and trans-8a, respectively, nL can be either C$_2$H$_4$ or 2PPh$_3$.

[13] The error was calculated using the law of error propagation.


[15] The following basis set was employed: 6-31G (d, p) for H, C, and O; Dev2-TZVP for P, Cl, and Br; Def2-TZVP with ECP for Pt and I.

[16] The reaction of trans-Pt(Cl)(C(O)C$_6$H$_4$Me-p)(PPh$_3$)$_2$ (trans-6c) with PhC(O)Br (2a) produced trans-Pt(Br)(C(O)C$_6$H$_4$Me-p)(PPh$_3$)$_2$ (trans-7c); however, neither trans-6a nor trans-7a was detected.

[17] Similarly, the reaction of trans-Pd(Cl)(C(O)Ph)(PPh$_3$)$_2$ (trans-9a) with p-MeC$_6$H$_4$C(O)Br (2c) selectively produced trans-Pd(Br)(C(O)Ph)(PPh$_3$)$_2$ (trans-10a).

[18] (a) Zhao, Y.; Truhlar, D. G. Theor. Chem. Acc. 2008, 120, 215. (b) The following basis set was employed: 6-31G (d, p) for Cl, Br, P, and C and O of the carbonyl group; STO-6G for C (except for C of carbonyl) and H; Lanl2DZ for Pt with ECP.


[22] (a) Cygan, Z. T.; Bender IV, J. E.; Litz, K. E.; Kampf, J. W.; Holl, M. M. B.

Chapter 2

Ligand Exchange Reaction of Aurous Complexes with Acid Halides

2-1 Introduction

One of the most common methods of preparation of transition-metal bromides and iodides is the conversion of the corresponding chlorides by the treatment with typical metal salts such as LiX, KX, and NaX (X = Br and I). In general, however, due to the necessity of employment of a large excess amount of metal salt and the formation of metal chloride as byproduct, a series of procedures such as filtration, extraction, drying with desiccant, and recrystallization are required to obtain analytically pure products. On the other hand, we have demonstrated in Chapter 1 that Cl-to-Br and Cl-to-I transformations of nickel triad complexes were quite facilely realized by using acetyl bromide and acetyl iodide as the halogen exchange reagents and analytically pure products were isolated by just subjection of the reaction mixture in vacuo. Herein, we wish to report that the prototype is also successfully applicable to the aurous complexes with the formula of Au(X)(L).\(^1\)

2-2 Results and Discussion

Into a Pyrex NMR glass tube were added Ph\(_3\)PAuCl (1a, 0.01 mmol), benzene-\(d_6\) (0.5 mL), MeC(O)Br (2, 0.012 mmol) at 25 °C. The \(^{31}\)P NMR spectrum taken right after the sample was prepared showed that 1a (\(\delta\) 33.4) was quantitatively converted into Ph\(_3\)PAuBr (3a) (\(\delta\) 35.2) (Eq. 1).

\[
\begin{align*}
\text{Ph}_3\text{PAuCl} & \quad + \quad \text{MeC(O)Br} \\
1a & \quad 0.01 \text{ mmol} & \quad 2 & \quad 1.2 \text{ equiv} \\
\text{benzene-}\text{d}_6 & \quad (0.5 \text{ mL}) & \quad \text{r.t., } < 15 \text{ min} & \quad \text{Ph}_3\text{PAuBr} & \quad + \quad \text{MeC(O)Cl}
\end{align*}
\]

In Chapter 1, we succeeded in demonstrating that the Cl-to-Br ligand exchange reaction between \(\text{trans-}\text{M(Cl)[C(O)Ph](PPh}_3)_2\) (M = Pt and Pd) and PhC(O)Br took place through \(\sigma\)-bond metathesis by density functional theory (DFT) method. Thus the reaction mechanism of the reaction of 1a with 2 was examined with the same calculation method (M06 functional).\(^2,3\) The study successfully located the transition state (TS7) of tricoordinated \(\sigma\)-bond metathesis. The energy diagram of the reaction pathway and the structure of TS7 are shown in Figures 1, respectively. It should be noted that the TS7 is only 5.9 kJ/mol energetically higher than the starting 1a and 2.
Figure 1. The energy diagram of the reaction of 1a with 2 via tricoordinated σ-bond metathesis and Structure of TS7 by DFT study with M06 functional.

The dihedral angle of \( \angle \text{Au-Cl-C-Br} \) of TS7 is 3.66°, demonstrating that σ-bond metathesis takes place through a slightly distorted quadrangular geometry. The selected bond lengths of reactants, products, and TS7 were shown in Figure 2. When the bond distance of Au-Cl of 1a (2.35 Å) is compared with that of TS7 (2.84 Å), the bond is stretched by 0.49 Å. On the other hand, C-Br bond difference between 2 (2.01 Å) and TS7 (2.26 Å) is only 0.25 Å. The bond length difference of C-Cl between TS7 (2.56 Å) and 4 (1.84 Å) is 0.72 Å, whereas Au-Br bond in TS7 (2.56 Å) shrinks by 0.13 Å with respect to that in 3a (2.43 Å). Therefore, both Au-Cl and C-Cl bonds undergo more dynamic bond changes than C-Br and Au-Br bonds. In other words, Cl atom takes a more roundabout route than Br atom during the course of σ-bond metathesis, a similar behavior found in the σ-bond metatheses of platinum and palladium complexes.

Figure 2. The selected bond lengths (Å) of starting materials, products, and TS7.
Figure 3. The possible Au(III) complexes.

For the halogen exchange reaction between 1a and 2, the mechanisms through Au(III) complexes such as square planer 8 and tetrahedral 9 are also possible as the intermediate or transition state by the oxidative addition of 2 to 1a (Figure 4). The DFT study suggested that the complex 8 could exist as an intermediate whose energy is 19.7 kJ/mol higher than starting 1a and 2. However, as we can see from the energy diagram shown in Figure 4, the transition state TS10 for the formation of 8 and TS11 from 8 to the products are 47.3 kJ/mol and 44.0 kJ/mol energetically higher than the reactants, respectively. On the other hand, all the attempts to locate 9 have failed by the DFT calculation. Based on these considerations, we concluded that the Cl-to-Br ligand exchange reaction between 1a and 2 proceeded through distorted σ-bond metathesis via TS7.

Figure 4. Calculated energy profile of the halogen exchange reaction between Au(Cl)(PPh₃) (1a) and MeC(O)Br (2) via square planar Au(III) complex (8).

To test the utility of the present transformation as the synthetic method, a large scale reaction was attempted as follows (Eq. 2 and 3). Into a 100 mL flask were added 1a (1.0 mmol), 2 (1.2 mmol) and C₆H₆ (50 mL) in a glove box at room temperature (Eq. 2). After the solution was stirred for 30 min, the solvent, excess 2 (b.p. 75-77 °C) and byproduct CH₃C(O)Cl (4, b.p. 52 °C) were removed in vacuo. The ³¹P and ¹H NMR spectra as well as elemental analysis of the product demonstrated that analytically pure 3a was obtained quantitatively. Similarly, Ph₃PAuI (5a) was isolated by a similar treatment of 1a with CH₃C(O)I (6, b.p. 108 °C).
Furthermore, the reactions of IPrAuCl (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene) (1b, 0.01 mmol) with 2 equiv of 2 and 6 in CD$_2$Cl$_2$ (0.5 mL) also facilely proceeded to afford IPrAuBr (3b) and IPrAuI (5b) quantitatively after 30 min at 25 °C, respectively (Eq. 3). Moreover preparative scale (0.5 mmol) reactions were successfully performed to afford 3b and 5b, respectively.

![Chemical Structure]

**2-3 Conclusions**

This study clearly suggested the generality of acetyl bromide (2) and iodide (6) as the convenient Cl-to-Br and Cl-to-I conversion reagents from metal chlorides through σ-bond metathesis mechanism.

**2-4 Experimental Section**

**General Comments**

The $^{31}$P and $^1$H NMR spectra in benzene-$d_6$ were measured with a JEOL JNM ECS400 (400 MHz) spectrometers. The chemical shifts of the $^{31}$P NMR spectra in benzene-$d_6$ were recorded relative to 85% H$_3$PO$_4$ (aq) as an external standard, Acetyl halides were commercially obtained. Benzene-$d_6$ was purified by distillation from sodium benzophenone ketyl before use. Au(Cl)(PPh$_3$) (1a) were prepared according to a literature. $^5$ Au(Cl)(IPr) were commercialy obtained. Registry No. of 1a: 14243-64-2; 3a: 14243-65-3; 5a: 21209-78-9; 1b: 852445-83-1; 3b: 932045-61-9; 5b: 1350769-89-9

1a: $^{31}$P NMR (160 MHz, C$_6$D$_6$) δ 33.41
3a: $^{31}\text{P}$ NMR (160 MHz, C$_6$D$_6$) $\delta$ 35.17
5a: $^{31}\text{P}$ NMR (160 MHz, C$_6$D$_6$) $\delta$ 39.69
1b: $^1\text{H}$ NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.57 (t, $J = 7.8$ Hz, 2 H), 7.35 (d, $J = 7.8$ Hz, 4 H), 7.23 (d, $J = 6.9$ Hz, 2H), 2.56 (sep, $J = 6.9$ Hz, 4 H), 1.34 (d, $J = 6.9$ Hz, 12 H), 1.23 (d, $J = 6.9$ Hz, 12 H)
3b: $^1\text{H}$ NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.56 (t, $J = 7.8$ Hz, 2 H), 7.35 (d, $J = 7.8$ Hz, 4 H), 7.23 (d, $J = 6.9$ Hz, 2H), 2.56 (sep, $J = 6.9$ Hz, 4 H), 1.33 (d, $J = 6.9$ Hz, 12 H), 1.22 (d, $J = 6.9$ Hz, 12 H)
5b: $^1\text{H}$ NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.56 (t, $J = 7.8$ Hz, 2 H), 7.34 (d, $J = 7.8$ Hz, 4 H), 7.23 (d, $J = 6.9$ Hz, 2H), 2.57 (sept, $J = 6.9$ Hz, 4 H), 1.33 (d, $J = 6.9$ Hz, 12 H), 1.22 (d, $J = 6.9$ Hz, 12 H)

Ligand Exchange Reaction between Cl of Au(Cl)(PPh$_3$) (1a) and Br of MeC(O)Br (2) (eq 1)

Into a dry Pyrex NMR tube were added 1a (4.9 mg, 0.010 mmol), MeC(O)Br (2, 1.5 mg, 0.012 mmol) and benzene-$_{d_6}$ (0.5 mL). The reaction at 25 °C was monitored by $^{31}\text{P}$ and $^1\text{H}$ NMR spectroscopies. Au(Br)(PPh$_3$) (3a) was generated quantitatively. A similar reaction of 1a with MeC(O)I (6) afforded Au(I)(PPh$_3$) (5a) quantitatively. The reactions using Au(Cl)(IPr) (1b) were performed similarly.

Preparative Scale Ligand Exchange Reaction

Into a 100 mL flask were added Au(Cl)(PPh$_3$) (1a, 772 mg, 1.0 mmol), MeC(O)Br (2, 492 mg, 4.0 mmol) and C$_6$H$_6$ (50 mL) in a glove box at room temperature. After the solution was stirred for 30 min, the solvent, excess 2 (b.p. 75-77 °C) and CH$_2$C(O)Cl (4, b.p. 52 °C) were removed in vacuo to give analytically pure 3a quantitatively (536 mg, 99%). Similarly, Au(I)(PPh$_3$) (5a) was isolated by the treatment of 1a with CH$_3$C(O)I (6, b.p. 108 °C) (587 mg, 100%). The reactions using Au(Cl)(IPr) (1b) were performed similarly. Into a 100 mL flask were added Au(Cl)(IPr) (1b, 311 mg, 0.5 mmol), 2 (123 mg, 1.0 mmol) and CH$_2$Cl$_2$ (25 mL) in a glove box at room temperature. After the solution was stirred for 1 h, the solvent, excess 2 and 4 were removed in vacuo to give analytically pure 3b quantitatively (333 mg, 100%). Similarly, Au(I)(IPr) (5a) was isolated by the treatment of 1a with 6 (352 mg, 99%).

Computational Details

The DFT calculations of the equilibrium structures and the energetics of the intermediates and transition states were carried out by the GAUSSIAN09 suite of programs. The following basis set was employed with M06 functional: 6-31G(d,p) for Cl, Br, and P atoms as well as C and O atoms of the carbonyl groups; STO-6G for all the atoms in the phenyl groups. The full
electron calculation for Au is rather time-consuming, so it is better to introduce effective core potentials including relativistic effects (RECP) for the Au (Xe core) atom in order to describe the inner core electrons. Under this approximation, the 19 valence electrons in the outer shell (5s5p5d6s) of the Au atom are described through the corresponding LanL2DZ basis sets. Geometry optimizations were performed without restricting the symmetry; all the calculations were performed under C1 symmetry. It was confirmed that all the intermediates are true local minima and all the transition states have only one imaginary frequency based on the vibrational analysis.

Table S1. The calculated energies of the reactants (1a and 2), TS7, intermediate (8) the transition states (TS10 and TS11), and products (3a and 4) for the halogen exchange reaction between Au(Cl)(PPh3) (1a) and Me(CO)Br (2). (1 a.u. = 2625.50 kJ/mol)

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<th>Compounds</th>
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<td>–</td>
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<td>Acetyl bromide (2)</td>
<td>-2724.70207200</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Au(Br)PPh₃ (3a)</td>
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<td>–</td>
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<tr>
<td>Acetyl chloride (4)</td>
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<td>–</td>
<td>–</td>
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<tr>
<td>Zero-point energy</td>
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<td>Acetyl bromide (2)</td>
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<td>–</td>
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<td>Au(Br)PPh₃ (3a)</td>
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<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Acetyl chloride (4)</td>
<td>-613.277769</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

σ-bond metathesis mechanism via tricoordinated complexes

| TS7                        | -4354.461509   | 129.7                   | 6.7         |
| Zero-point energy          |                |                         |             |
| TS7                        | -4354.123633   | 129.7                   | 5.9         |

Mechanism via square planar complex

| TS10                       | -4354.445310   | 169.4                   |             |
| 8                          | -4354.457099   | –                       | –           |
| TS11                       | -4354.446343   | 206.4                   |             |

Zero-point energy

| TS10                       | -4354.107914   | 169.4                   | 47.3        |
| 8                          | -4354.118429   | –                       | –           |
| TS11                       | -4354.109114   | 206.4                   | 24.3        |
Structures of reactants, intermediates, transition states, and products

1a

3a

TS7

TS10

8
3-5 References and Notes


[3] (a) Zhao, Y.; Truhlar, D. G. Theor. Chem. Account 2008, 120, 215. (b) The following basis sets were employed: 6-31G (d,p) for Cl, Br, P and C and O of the carbonyl group; STO-6G for H and C of phenyl group; Lanl2DZ for Au with ECP.

Chapter 3

Ligand Exchange Reaction of Ruthenium Complexes with Acid Halides

3-1 Introduction

Author has described that the ligand exchange reaction between M-X bonds of trans-M(X)[C(O)Ar](PPh$_3$)$_2$ and C-X' bonds of ArC(O)X' (M = Pt, Pd; X, X' = Cl, Br, I) successfully occurred to give a clean equilibrium mixture of trans-M(X)[C(O)Ar](PPh$_3$)$_2$/ArC(O)X' and trans-M(X')[C(O)Ar](PPh$_3$)$_2$/ArC(O)X in Chapter 1. Similarly, the conversion of Au(L)Cl (L = PPh$_3$, IPr) to the corresponding bromide and iodide was achieved, and a σ-bond metathesis was also identified by theoretical calculation (Chapter 2). This transformation benefits from its simple handling. Analytically pure products were obtained successfully just by mixing of reagents and the subsequent removal of the solvent, by-product (MeC(O)Cl), and excess MeC(O)X by evaporation. Procedures that are usually required in conventional syntheses involving typical LiX, KX, and NaX metal salts, such as filtration, extraction, drying in the presence of desiccant, and recrystallization, were omitted. Herein, the Cl-to-X conversion of a ruthenium chloride is described along with its mechanistic study.  

3-2 Results and Discussion

The reaction of CpRu(Cl)(PPh$_3$)$_2$ (1, 0.010 mmol) with MeC(O)Br (2, 0.020 mmol) in C$_6$D$_6$ (0.75 mL) at room temperature was monitored by $^{31}$P and $^1$H NMR spectroscopies (Eq. 1). The gradual clean conversion of 1 ($\delta$ 40.1) to CpRu(Br)(PPh$_3$)$_2$ (3) ($\delta$ 39.0) and MeC(O)Cl (4) was observed (6.3% of 3 after 0.5 h). After 9 h, 3 was produced quantitatively. No intermediate was detected during the course of the reaction. A similar treatment of 1 with MeC(O)I (5) produced CpRu(I)(PPh$_3$)$_2$ (6) ($\delta$ 38.0) after 2.5 h at room temperature.

\begin{align*}
\text{CpRu(Cl)(PPh$_3$)$_2$} + \text{MeC(O)X} \rightarrow \text{CpRu(X)(PPh$_3$)$_2$} + \text{MeC(O)Cl} \\
(1)
\end{align*}

Next, preparative scale reactions were executed to demonstrate the utility of the present reaction as a synthetic method. Compound 1 (1.0 mmol) and 2 (5.0 mmol) were added to C$_6$H$_6$ (50 mL) in a 100 mL flask fitted with a stirring bar in a glove box. After the reaction mixture was stirred at 25 °C for 3 h, the solvent, excess 2 (b.p. 75-77 °C), and 4 (b.p. 52 °C) were
removed in vacuo. NMR spectra and elemental analysis showed that analytically pure 3 was obtained. A similar large scale reaction was conducted with 5 at 25 °C for 4 h to quantitatively afford 6.

The mechanism of the reaction between 1 and 2 was theoretically investigated DFT using the M06 functional.\(^5\)\(^6\) This computational method was shown to give reliable geometries and energies in Chapter 1 and 2 on the ligand exchange reactions of trans-M(Cl)[C(O)Ph](PPh\(_3\))\(_2\) (M = Pt, Pd) and Au(Cl)(PPh\(_3\)) with RC(O)Br (R = Ph, Me). Three possible reaction pathways are shown in Scheme 1. In mechanism 1, The liberation of PPh\(_3\) produces the coordinately unsaturated CpRu(Cl)(PPh\(_3\)) (7). Next, \(\sigma\)-bond metathesis between the Ru-Cl bond of 7 and the C-Br bond of 2 affords TS1, and the subsequent elimination of 4 yields CpRu(Br)(PPh\(_3\)) (8), which can undergo recoordination by PPh\(_3\) to form 3. The associative elimination of PPh\(_3\) to form 9 before TS1 formation is considered in Mechanism 2. Mechanism 3 involves the oxidative addition of the Br-C bond to 9 that produces Ru(IV) complex 10.\(^7\)

\[\text{Scheme 1. Possible reaction pathways of the reaction between 1 and 2.}\]

In addition to the species shown in Scheme 1, the study identified transition states TS2, TS3, TS4 and TS5. The energy diagram and optimized transition state and intermediate structures are shown in Figure 1. The energy of TS2, which leads to the formation of 9, was 101.6 kJ/mol higher than the reactants. On the other hand, the formation of 7 required 147.5 kJ/mol, which was clearly energetically more demanding. Similarly, the energy of 8 (128.3 kJ/mol) was much higher than that of TS5 (95.6 kJ/mol), which generates 3 by elimination 4. Therefore, we concluded that Mechanism 1 is unlikely. In intermediate 9 (79.2 kJ/mol), one hydrogen of Me of the incoming acetyl bromide is found in close proximity to the Cl atom, hydrogen bond-like interaction as suggested by the Cl…H (2.53 Å). Two pathways were considered from 9: The \(\sigma\)-bond metathesis that provides 11 via the transition state TS1 (Mechanism 2), and the oxidative addition of Br-C bond, which yields Ru(IV) complex 10 via
TS3 followed by the Cl-C bond-forming reductive elimination to afford 11 via TS4 (Mechanism 3). The energies of TS1 and 11 amounted to 117.9 and 72.3 kJ/mol, respectively. The energies of TS3, 10, and TS4 equaled 124.7, 93.6 and 117.5 kJ/mol, respectively. The energy of TS1 was 6.8 kJ/mol lower than that for TS3, suggesting that Mechanism 2 was more favorable than Mechanism 3. After the formation of 11, in which the Br…H distance is 2.53Å, the associative elimination of 4 via TS5 (95.6 kJ/mol) produced 3 and 4. A total energy change of -15.5 kJ/mol was calculated for the entire reaction (ΔG = -16.0 kJ/mol). In TS2, dihedral angles ∠Ru-Cl-C-O and ∠Ru-Br-C-O equaled -179.4° and 179.9°, respectively. Likewise, in TS5, the dihedral angles ∠Ru-Cl-C-O and ∠Ru-Br-C-O equaled -179.9° and 177.8°, respectively. This shows that Ru, Cl, C, O of the carbonyl group, and Br atoms are nearly coplanar in TS2 and TS5. On the other hand, the dihedral angles ∠Ru-Cl-Br-C of TS2, 9, TS1, 11, and TS5 amounted to 179.8°, 116.0°, 137.9°, 104.0°, and 179.9°, respectively. Therefore, the Ru-Cl-C-Br quadrangle bends downward from flat TS2 to 9, and flips back to TS1 before bending downward again to 11 and flattening again to TS5. The dihedral angle ∠Ru-Cl-Br-C of TS3, 10, and TS4 equaled 102.1°, 104.8°, and 93.6° in TS3, 10, and TS4, respectively, suggesting that this quadrangle folded similarly to the Ru-Cl-C-Br quadrangle. However, this movement in Mechanism 3 was less dynamic than in the of σ-bond metathesis mechanism. The C=O group gradually changed direction from right to left in both mechanisms during this folding process (Figure 1).

Figure 1. Energy diagram for the reaction of 1 with 2. Phenyl of PPh₃ and hydrogen atoms of Cp are omitted for clarity. Atoms in blue, orange, green, dark red, and red represent Ru, P, Cl, Br, and O, respectively.
Besides those shown in Scheme 1, another possible reaction mechanism involves the formation of the 18-electron cationic complex 12 (L' = PPh$_3$ or solvent), which reacts with 2 to provide 13, and the subsequent elimination of L' to form 3. If the reaction proceeded via 12, the addition of free PPh$_3$ or acetonitrile would accelerate the reaction. However, the transformation was actually rather suppressed by the addition of PPh$_3$ (0.1 equiv) under the same conditions, excluding the formation of 12 and this mechanism. This retardation is consistent with Mechanism 2, which involves the elimination of PPh$_3$.

Scheme 2. Another possible mechanism via cationic complexes.

In stark contrast to halogen-exchange reactions of Platinum, Palladium and Aurous complexes in chapter 1 and 2, the radical and radical inhibitor remarkably affected the present Ru-system. The reaction of 1 with 2 in the presence of 0.1 equiv of TEMPO under otherwise similar conditions only gave 19% of 3 after 9 h (Eq. 3), compare this with the result of Eq. 2. On the other hand, the same reaction in the presence of 1.0 equiv of 9,10-dihydroanthracene (DHA) produced 3 in 75% after 0.5 h and quantitatively within 2 h. These results clearly show the participation of a radical species in the reaction mechanism. Reports have shown that Cp*Ru(Cl)(PPh$_3$)$_2$, an analog of 1, subtracted a halogen from halogenated compounds during the process of the atom transfer radical addition (ATRA) to alkenes. A revised mechanism is therefore proposed in Scheme 3. After the formation of 9 via TS2, the Br atom is subtracted by the Ru atom to give radical pair 14 consisting of a Ru(III) fragment and an acetyl radical. Subsequent Cl atom subtraction by the acetyl radical would afford 11. This process could be affected by the radical inhibitor or promoter. The energy of 14 would be lower than TS1. In fact, the combined energy of CpRu(Cl)(Br)(PPh$_3$) and CH$_3$C(O)· is 71.4 kJ/mol, implicating the presence of radical process with lower energy.
Scheme 3. A revised mechanism via radical pair species

3-3 Conclusions

This paper clearly demonstrates acetyl bromide (2) and iodide (5) as convenient Cl-to-Br and Cl-to-I conversion reagents in CpRu(Cl)(PPh₃)$_2$ reaction. Moreover, DFT calculations suggest that the associative liberation of PPh₃ before the generation of associated complex intermediate. The significant influence by the radical inhibitor and promoter suggests the participation of the radical species during the process.

3-4 Experimental Section

Genaral Comments

The $^{31}$P and $^1$H NMR spectra in benzene-$d_6$ were measured with a ECS400 (400 MHz) spectrometer. The chemical shifts of the $^{31}$P NMR spectra in benzene-$d_6$ were recorded relative to 85% H$_3$PO$_4$ (aq) as an external standard, and S=P(C₆H₄OMe-p)$_3$ was used as an internal standard to calculate the yields of products (The sensitivities of ruthenium complexes to the internal standard were measured individually). Acetyl halides and benzoyl bromide were commercially obtained. Benzene-$d_6$ was purified by distillation from sodium benzophenone ketyl before use. CpRu(Cl)(PPh₃)$_2$ (1) was prepared according to a literature.$^{11}$ Registry No. of 1: 32993-05-8; 3: 32993-06-9; 6: 34692-10-9

1: $^{31}$P NMR (160 MHz, C₆D₆) δ 40.10, 3: $^{31}$P NMR (160 MHz, C₆D₆) δ 38.97, 6: $^{31}$P NMR (160 MHz, C₆D₆) δ 37.97
A ligand exchange reaction between Cl of CpRu(Cl)(PPh\textsubscript{3})\textsubscript{2} (1) and Br of MeC(O)Br (2) (Eq. 2)

Into a dry Pyrex NMR tube were added a solution of CpRu(Cl)(PPh\textsubscript{3})\textsubscript{2} (1, 0.010 mmol, 500 \mu L/20 mM in benzene-\textit{d\textsubscript{6}}), a solution of S=P(C\textsubscript{6}H\textsubscript{4}OMe-p)\textsubscript{3} (0.0050 mmol, 50 \mu L/100 mM in benzene-\textit{d\textsubscript{6}}), and benzene-\textit{d\textsubscript{6}} (180 \mu L). After the sensitivity of 1 to the internal standard was measured by \textsuperscript{31}P NMR spectroscopy, a solution of MeC(O)Br (2, 0.020 mmol, 20 mL/1.0 M in benzene-\textit{d\textsubscript{6}}) was added and the reaction was monitored by \textsuperscript{31}P NMR spectroscopy. The gradual conversion of 1 to 3 was confirmed. The reaction time and yield are as follows: 0.5 h, 6.3%; 1 h, 15%; 2 h, 38%; 3 h, 62%; 4 h, 80%; 5 h, 90%; 6 h, 95%; 7 h, 98%; 8 h, 99%; 9 h, 100%.

Preparative scale ligand exchange reactions

Into a 100 mL flask were added CpRu(Cl)(PPh\textsubscript{3})\textsubscript{2} (1, 726.2 mg, 1.0 mmol), MeC(O)Br (2, 614.8 mg, 5.0 mmol), and C\textsubscript{6}H\textsubscript{6} (50 mL) in a glove box at room temperature. After the solution was stirred for 3 h, the solvent, excess 2 (b.p. 75-77 °C) and MeC(O)Cl (4, b.p. 52 °C) were removed in vacuo to give analytically pure 1 quantitatively (764.8 mg, 99%). Similarly, CpRu(I)(PPh\textsubscript{3})\textsubscript{2} (6) was isolated by the treatment of 1 with MeC(O)I (5, b.p. 108 °C) (812.5 mg, 99%)

Effect of Addition of PPh\textsubscript{3}

Into a dry Pyrex NMR tube were added a solution of CpRu(Cl)(PPh\textsubscript{3})\textsubscript{2} (1, 0.010 mmol, 500 \mu L/20 mM in benzene-\textit{d\textsubscript{6}}), a solution of S=P(C\textsubscript{6}H\textsubscript{4}OMe-p)\textsubscript{3} (0.0050 mmol, 50 \mu L/100 mM in benzene-\textit{d\textsubscript{6}}), a solution of PPh\textsubscript{3} (0.0010 mmol, 10 \mu L/100 mM in benzene-\textit{d\textsubscript{6}}), and benzene-\textit{d\textsubscript{6}} (170 \mu L). After the sensitivity of 1 to the internal standard was measured by \textsuperscript{31}P NMR spectroscopy, a solution of MeC(O)Br (2, 0.020 mmol, 20 mL/1 M in benzene-\textit{d\textsubscript{6}}) was added and the reaction was monitored by \textsuperscript{31}P NMR spectroscopy and the result was compared with that of the reaction carried out without the addition of free PPh\textsubscript{3} (Figure S1), demonstrating that the ligand exchange reaction is retarded by the addition of PPh\textsubscript{3}.

Figure S1

<table>
<thead>
<tr>
<th>time (hrs)</th>
<th>yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>80</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>

- 42 -
Effect of Addition of TEMPO or DHA (9,10-dihydroanthracene) (Eq3)

The reactions were performed similarly in the presence of 0.1 equiv of TEMPO or 1 equiv of DHA instead of PPh3. The reaction times and yields are as follows: TEMPO: 1 h, 3%; 3 h, 9%; 6 h, 13%; 9 h, 19%. DHA: 30 min, 75%; 1 h, 99%; 2 h, 100%.

Computational details

All the calculations in this study were performed using the GAUSSIAN 09 suite of programs.1 We applied the M06 functional, which has demonstrated as a useful functional for investigating chemical processes of transition metal chemistry.5,6 The effective core potentials including relativistic effects (RECP) was employed to describe the inner core electrons for the Ru (Kr core). Under this approximation, the 16 valence electrons in the outer shell (4p4d5s) of the Ru atom are described through the corresponding LanL2DZ basis set. The 6-31G(d,p) basis sets were employed for cyclopentadienyl ligand, phosphorus atom of PPh3, Cl, Br, and carbon and oxygen atoms of carbonyl group of acetyl bromide and acetyl chloride. The STO-6G basis sets were applied for phenyl group of PPh3 and methyl group of acetyl bromide and acetyl chloride. During the optimization, all the molecular structures were fully relaxed without any symmetry constraints. All the ground state structures optimized are local minima; vibrational analyses performed at the optimized structures contained no imaginary frequencies. All the optimized transition state structures possessed only one imaginary frequency. The IRC calculations were performed and the key transition states were verified. The forward and reverse IRC followed for 50 steps along the reaction pathway.

Table S1. Selected angles (degree) and distances (Å).

<table>
<thead>
<tr>
<th>parameters</th>
<th>TS2</th>
<th>9</th>
<th>TS1</th>
<th>TS3</th>
<th>11</th>
<th>10</th>
<th>TS5</th>
<th>TS4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;Ru-Cl-Br-C</td>
<td>179.8</td>
<td>116.0</td>
<td>137.9</td>
<td>102.1</td>
<td>104.0</td>
<td>104.8</td>
<td>179.9</td>
<td>93.6</td>
</tr>
<tr>
<td>&lt;Cl-Ru-Br</td>
<td>99.3</td>
<td>85.2</td>
<td>79.2</td>
<td>123.4</td>
<td>59.5</td>
<td>139.7</td>
<td>102.4</td>
<td>123.0</td>
</tr>
<tr>
<td>&lt;Cl-C-Br</td>
<td>76.1</td>
<td>79.2</td>
<td>92.7</td>
<td>104.5</td>
<td>86.2</td>
<td>108.5</td>
<td>67.8</td>
<td>101.9</td>
</tr>
<tr>
<td>Ru-Cl</td>
<td>2.66</td>
<td>2.46</td>
<td>2.67</td>
<td>2.41</td>
<td>3.27</td>
<td>2.48</td>
<td>2.78</td>
<td>2.79</td>
</tr>
<tr>
<td>Ru-Br</td>
<td>3.33</td>
<td>3.19</td>
<td>2.76</td>
<td>2.84</td>
<td>2.56</td>
<td>2.55</td>
<td>2.86</td>
<td>2.52</td>
</tr>
<tr>
<td>Cl-C</td>
<td>4.62</td>
<td>3.69</td>
<td>2.35</td>
<td>3.54</td>
<td>1.86</td>
<td>2.79</td>
<td>1.90</td>
<td>2.11</td>
</tr>
<tr>
<td>Br-C</td>
<td>2.05</td>
<td>2.03</td>
<td>2.43</td>
<td>2.23</td>
<td>4.13</td>
<td>3.03</td>
<td>4.75</td>
<td>3.76</td>
</tr>
<tr>
<td>Ru-C</td>
<td>4.54</td>
<td>3.77</td>
<td>3.49</td>
<td>2.49</td>
<td>3.80</td>
<td>2.10</td>
<td>4.23</td>
<td>2.46</td>
</tr>
</tbody>
</table>
Table S2. The calculated total energies of the reactants, the transition states, intermediates, and products for the halogen exchange reaction between CpRu(Cl)(PPh$_3$)$_2$ (1) and MeC(O)Br. (1 a.u. = 2625.5 kJ mol$^{-1}$)

<table>
<thead>
<tr>
<th>compounds</th>
<th>$E$ (a.u.)</th>
<th>$E_{ZPE}^{\text{a}}$ (a.u.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CpRu(Cl)(PPh$_3$)$_2$ (1) (Cs)</td>
<td>-2815.56602</td>
<td>-2814.90177</td>
</tr>
<tr>
<td>MeC(O)Br (2)</td>
<td>-2724.31386</td>
<td>-2724.26448</td>
</tr>
<tr>
<td><strong>TS2</strong></td>
<td>-5539.83805</td>
<td>-5539.12756</td>
</tr>
<tr>
<td><strong>9</strong></td>
<td>-4505.82482</td>
<td>-4505.40059</td>
</tr>
<tr>
<td><strong>TS1</strong></td>
<td>-4505.80813</td>
<td>-4505.38583</td>
</tr>
<tr>
<td><strong>11</strong></td>
<td>-4505.82888</td>
<td>-4505.40322</td>
</tr>
<tr>
<td><strong>TS5</strong></td>
<td>-5539.84505</td>
<td>-5539.12984</td>
</tr>
<tr>
<td>MeC(O)Cl (4)</td>
<td>-613.23369</td>
<td>-613.18371</td>
</tr>
<tr>
<td>CpRu(Br)(PPh$_3$)$_2$ (3) (Cs)</td>
<td>-4926.65266</td>
<td>-4925.98845</td>
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<tr>
<td>PPh$_3$</td>
<td>-1034.02569</td>
<td>-1033.73551</td>
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<td>CpRu(Cl)(PPh$_3$)$_2$ (7)</td>
<td>-1781.48250</td>
<td>-1781.11010</td>
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<tr>
<td>CpRu(Br)(PPh$_3$)$_2$ (8)</td>
<td>-3892.57022</td>
<td>-3892.19816</td>
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<tr>
<td><strong>TS3</strong></td>
<td>-4505.80740</td>
<td>-4505.38326</td>
</tr>
<tr>
<td><strong>10</strong></td>
<td>-4505.81909</td>
<td>-4505.39510</td>
</tr>
<tr>
<td><strong>TS4</strong></td>
<td>-4505.81061</td>
<td>-4505.38600</td>
</tr>
<tr>
<td><strong>14</strong></td>
<td>-4352.83229</td>
<td>-4352.45495</td>
</tr>
<tr>
<td>MeCl(O)</td>
<td>-152.99438</td>
<td>-152.94855</td>
</tr>
</tbody>
</table>

*a* with zero-point energy correction

**IRC analysis**

**Figure S2.** From 9 to 11 via TS1.
Figure S3. The IRC energy diagram of the transformation from 9 to 10 via TS3.

Figure S4. The IRC energy diagram of the transformation from 10 to 11 via TS4.

Structures of reactants, intermediates, transition states, and products

1

TS2

9

TS1

11
3-5 References and Notes


4-1 Introduction

Organic fluorine compounds play an important role in pharmaceuticals, agrochemicals, materials and tracers for positron emission tomography (PET), because the unique nature of fluorine critically affects the changing of chemical, biological and physical properties.\textsuperscript{1} Fluoroalkene moiety is regarded as peptide mimics, therefore it has potential applications in medicinal chemistry.\textsuperscript{2}

It is known that the addition reaction of the acid chloride to alkynes takes place by using transition-metal catalysts\textsuperscript{3} or Lewis acids\textsuperscript{4}. However, additions of the acid fluoride to alkynes have not been development despite the usefulness of fluoroalkene which could be afforded by such reactions. Herein, we report Lewis acid catalyzed intramolecular acylfluorination of alkynes: this is the first protocol demonstrated for a direct addition of C-F bond to unsaturated C-C bond (Eq 1).

\[
\begin{align*}
\text{O} & \quad \text{Ph} \\
& \quad \text{Lewis acid} \\
\text{F} & \quad \text{Ph} \\
\end{align*}
\]

\text{(1)}

4-2 Results and Discussion

Initially we treated the acid fluoride 1a bearing alkyne moiety using 10 mol\% of BF\textsubscript{3}-OEt\textsubscript{2} as a Lewis acid with stirring for 12 hours and afforded the desired product 2a in 94\% yield with \(E/Z = 3:1\) selectivity (Table 1, entry 1). When the reaction time was shorten from 12 to 2 hours, the yield of 2a was decreased (entry 2). However, the \(E/Z\) selectivity of 2a was improved to 8.6:1. The reaction performed by use of 10 mol\% catalyst lording for 2 h gave 2a in high yield (91\%) and high selectivity (\(E/Z = 5.5:1\)) (entry 3). When B(OEt)\textsubscript{3} and BPh\textsubscript{3} were used as a Lewis acid catalyst, the product 2a were gained in only trace amount (entries 4 and 5). The use of B(C\textsubscript{6}H\textsubscript{5})\textsubscript{3} was less efficient in the acylfluorination of 1a than the use of BF\textsubscript{3}-OEt\textsubscript{2} (entry 6). Non-boron-based Lewis acid such as AlCl\textsubscript{3}, FeCl\textsubscript{3}, ZnCl\textsubscript{2} did not show a good activity in the acylfluorination (entries 7, 8 and 9).

To gain insight into the mechanism of the acylfluorination, we examined the reaction of \(E-2a\), which was isolated by the fluoroacylation of 1a, in the presence of BF\textsubscript{3}-OEt\textsubscript{2} in CD\textsubscript{2}Cl\textsubscript{2} at room temperature by \(^{19}\text{F}\) NMR spectroscopy (Eq 2). After 11 hours, isomerization of \(E-2a\) was observed to give the mixture of the isomers (\(E/Z = 2.2/1\)). On the other hand, in the absence of the catalyst, no isomerization was observed. This result shows that the isomerization of \(E-2a\) was promoted by BF\textsubscript{3}-OEt\textsubscript{2} and that present acylfluorination kinetically
proceeds in a trans addition manner to afford \( E-2a \), followed by isomerization of \( C=C \) double bond of \( E-2a \) to yield \( Z-2a \).

**Table 1. Optimization of the Reaction Conditions**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Lewis Acid</th>
<th>Catalyst Lording [mol%]</th>
<th>( t ) [h]</th>
<th>Yield [%] (^a)</th>
<th>( E/Z ) (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BF(_3)•OEt(_2)</td>
<td>5</td>
<td>12</td>
<td>94</td>
<td>3/1</td>
</tr>
<tr>
<td>2</td>
<td>BF(_3)•OEt(_2)</td>
<td>5</td>
<td>2</td>
<td>67</td>
<td>8.6/1</td>
</tr>
<tr>
<td>3</td>
<td>BF(_3)•OEt(_2)</td>
<td>10</td>
<td>2</td>
<td>91</td>
<td>5.5/1</td>
</tr>
<tr>
<td>4</td>
<td>B(OEt)(_3)</td>
<td>10</td>
<td>12</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>BPh(_3)</td>
<td>10</td>
<td>12</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>B(C(_6)F(_5))(_3)</td>
<td>10</td>
<td>12</td>
<td>52</td>
<td>2/1</td>
</tr>
<tr>
<td>7</td>
<td>AlCl(_3)</td>
<td>10</td>
<td>12</td>
<td>8</td>
<td>1/1</td>
</tr>
<tr>
<td>8</td>
<td>FeCl(_3)</td>
<td>10</td>
<td>12</td>
<td>28</td>
<td>2.1/1</td>
</tr>
<tr>
<td>9</td>
<td>ZnCl(_2)</td>
<td>10</td>
<td>12</td>
<td>trace</td>
<td>-</td>
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</table>

DCM = dichloromethane \(^a\) Yields and ratios of \( E/Z \) were determined by \(^{19}\)F NMR using PhF as an internal standard.

A proposed mechanism of the acylfluorination is shown Scheme 1. Initially, BF\(_3\) abstracts F\(^-\) anion of \( 1a \) to generate the acyl cation intermediate 3 and BF\(_4\)\(^-\). Then, the intramolecular reaction of acyl cation with alkyne undergoes to form vinyl cation intermediate 4. Finally, 4 is fluorinated by BF\(_4\)\(^-\) to form \( E-2a \) and regenerate BF\(_3\), where BF\(_3\)\(^-\) anion approaches to the opposite side of the carbonyl group due to its electronic and steric hindrance.

The results of the intramolecular acylfluorinations of various substrates \( 1a-g \) are summarized in Table 2. The reaction of substrate \( 1b \) bearing electron-poor aryl group (\( p-CF_3-C_6H_4 \)) in the presence of 10 mol\% of BF\(_3\)•OEt\(_2\) for 12 hours afforded the desired product \( 2b \) in 68\% isolated yield (\( E/Z = 4.3/1 \)). On the other hand, the reaction of substrate \( 1c \) having electron-rich aryl group (\( p-MeO-C_6H_4 \)) afforded the desired adduct \( 2c \) in only trace yield. The reaction of oxygen-tethered substrate \( 1d \) in the presence of 10 mol\% of BF\(_3\)•OEt\(_2\) for 24 hours produced \( 2d \) in 87\% yield with high selectivity (\( E/Z = 18/1 \)). Similarly, use of the substrate (\( 1e \))
containing NTs tether in the arm resulted in high selectivity \((E/Z = >99/1)\). In the cases of substrates with shorter or longer alkyl chain than \(1a\), the acylfluorination products (\(2f\) or \(2g\)) were not yielded.

Scheme 1. Proposed Mechanism for the Intramolecular Acylfluorination

Table 2. Scope and Limitations\(^a\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>E/Z</th>
<th>Time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2a)</td>
<td>85%(^b)</td>
<td>5.5/1</td>
<td>2</td>
</tr>
<tr>
<td>(2b)</td>
<td>68%(^b)</td>
<td>4.3/1</td>
<td>12</td>
</tr>
<tr>
<td>(2c)</td>
<td>Trace</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>(2d)</td>
<td>87%(^b)</td>
<td>18/1</td>
<td>24</td>
</tr>
<tr>
<td>(2e)</td>
<td>68%(^b)</td>
<td>&gt;99/1</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^a\) \(1\) (0.5 mmol), \(\text{BF}_3\)\(\cdot\)\(\text{OEt}_2\) (10 mol\%), and DCM (10 mL) at r.t.

\(^b\) Isolated yield

\(^c\) 40 mol\% of \(\text{BF}_3\)\(\cdot\)\(\text{OEt}_2\)
4-3 Conclusions

We demonstrated the intramolecular fluoroacylation of alkynes was achieved by employing BF$_3$·OEt$_2$ as a Lewis acid catalyst and acid fluorides bearing alkyne moieties as substrates. The reaction sequence proceeded in a trans-addition manner, followed by isomerization of double bond of the product.

4-4 Experimental Section

General Comments

The $^1$H, $^{13}$C and $^{19}$F NMR spectra in CDCl$_3$ and CD$_2$Cl$_2$ were measured with a ECS400 (400 MHz) spectrometer. The chemical shifts in the $^1$H NMR spectra were recorded relative to Me$_4$Si as an internal standard, and the chemical shifts in the $^{13}$C NMR spectra were recorded relative to CHCl$_3$ (δ 77.0). CD$_2$Cl$_2$ was purified by distillation from P$_2$O$_5$ before use.

Typical Procedure for the Intramolecular Acylfluorination (1a)

Into a reaction glass equipped with a magnetic stirring bar were added 5-phenyl-4-pentynoyl fluoride (1a, 0.5 mmol, 95.1 mg), DCM (10 mL), BF$_3$·OEt$_2$ (0.05 mmol), and the reaction mixture was stirred for 2 hrs at room temperature and then was quenched by sat. NaHCO$_3$. The resulting mixture was poured sat. NaCl and extracted with Et$_2$O. The organic layer was dried over Na$_2$SO$_4$, and the solvent was removed under reduced pressure to afford the crude product, which was analyzed by NMR spectroscopy. NMR Yields and ratios of E/Z were determined by $^{19}$F NMR using PhF as an internal standard. The product was purified by silicagel column chromatography.

E-2a: 72% yield; pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.78 (m, 2H), 7.44 (m, 3H), 2.95 (dt, $J = 7.3$, 3.2, 2H), 2.44 (t, $J = 7.8$, 2H), 1.95 (m, 2H); $^{19}$F NMR (376 MHz, CDCl$_3$) δ -76.83 (s)

Z-2a: 12% yield; a pale yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (m, 2H), 7.47 (m, 3H), 2.92 (dt, $J = 6.9$, 3.2, 2H), 2.42 (t, $J = 7.8$, 2H), 2.00 (m, 2H); $^{19}$F NMR (376 MHz, CDCl$_3$) δ -97.23 (s)

Typical Procedure for Synthesis of Acid Fluoride 1a

To a solution of 6-phenyl-5-hexynoic acid (1.74 g, 10 mmol) in dichloromethane (10 mL) was slowly added DAST (1.93 g, 12 mmol) at 0 ºC and the reaction mixture was stirred for 15 min at room temperature. Then, the mixture was diluted with pentane. The organic phase was washed with cold water and dried over MgSO$_4$. The solvent was condensed under reduced pressure to give the product (orange oil, 1.65, 95%). $^1$H NMR (400 MHz, CDCl$_3$): δ 1.98 (m, $J = 6.8$ Hz, 2H), δ 2.56 (t, $J = 6.4$ Hz, 2H), δ 2.74 (t, $J = 7.3$ Hz, 2H), δ 7.28-7.40 (m, 5H). $^{19}$F
NMR (376 MHz, CDCl₃): δ 45.95.

4-5 References and Notes


Summary

In this thesis, the studies on the halogen-exchange reaction between various transition-metal complexes and acid halides and Lewis acid catalyzed intramolecular addition of acid fluoride to alkynes are described. The results are summarized as follows.

In chapter 1, the efficiently halogen exchange reactions between palladium/platinum complexes and acid halides are described. The reaction between \( \text{trans-M(X)[C(O)Ph](PPh}_3\text{)}_2 \) and \( \text{PhC(O)X}' \) (M = Pt, Pd; X, X’ = Cl, Br, I) successfully gave a clean equilibrium mixture. The Gibbs free energy (\( \Delta G_s \)) was equivalent to the \( \Delta\Delta G \) of the oxidative additions of \( \text{PhC(O)X} \) and \( \text{PhC(O)X}' \) to \( \text{M(PPh}_3\text{)}_2\text{Ln} \) (\( \text{Ln} = 2\text{PPh}_3 \) or \( \text{CH}_2\text{=CH}_2 \)). Both experimental and computational studies supported the concerted \( \sigma \)-bond metathesis mechanism. The reaction are used as a very convenient method to convert Cl ligand into Br and I ligands by using acetyl halides.

In chapter 2, the halogen exchange reactions between aurous complexes and acid halides are described. The complexes of the formula \( \text{Au(X)(L)} \) (X = Br and I; L = \( \text{PPh}_3 \) and IPr) were conveniently prepared by a quite simple procedure using the treatment of \( \text{Au(Cl)(L)} \) with \( \text{CH}_3\text{C(O)X} \). The mechanistic study by DFT calculation supported that the reaction proceeded through the concerted \( \sigma \)-bond metathesis.

In chapter 3, the halogen exchange reactions between ruthenium complexes and acid halides are described. The treatment of \( \text{CpRu(Cl)(PPh}_3\text{)}_2 \) with \( \text{MeC(O)X} \) provides a very convenient procedure for the synthesis of \( \text{CpRu(X)(PPh}_3\text{)}_2 \). The proposed mechanism involves an intermediate produced by the concerted liberation of \( \text{PPh}_3 \) by the incoming \( \text{MeC(O)X} \) and the subsequent subtraction of the X atom by the Ru atom to form a radical pair in stark contrast to halogen-exchange reactions of Pt, Pd and Au complexes described in chapters 1 and 2.

In chapter 4, Lewis acid (\( \text{BF}_3\cdot\text{OEt}_2 \)) catalyzed intramolecular acyl fluorination of alkynes is described. This transformation was successfully applied to the construction of a cyclopentanones bearing vinyl fluoride moiety.

These aspects would be good representations showing great potential of the reactions utilizing acid halides for transformations of transition-metal complexes and catalytic reactions.
List of Publications

1. σ-Bond Metathesis between M-X and RC(O)X’ (M = Pt, Pd; X, X’ = Cl, Br, I): Facile Determination of the Relative ΔG Values of the Oxidative Addition of RC(O)X to an M(0) Complex, Evidence by Density Functional Theory Calculations, and Synthetic Applications
   Hitoshi Kuniyasu, Atsushi Sanagawa, Daisuke Nakane, Takanori Iwasaki, Nobuaki Kambe, Karan Bobuatong, Yunpeng Lu, and Masahiro Ehara

2. Facile Halogen Exchange Method between Au(Cl)(L) and MeC(O)X (L = PPh$_3$ and IPr; X = Br and I) via σ-Bond Methathesis Supported by DFT Calculation
   Atsushi Sanagawa, Hitoshi Kuniyasu, Takanori Iwasaki, Nobuaki Kambe, Karan Bobuatong, and Masahiro Ehara

3. Halogen Exchange by Reaction of CpRu(Cl)(PPh$_3$)$_2$ with MeC(O)X (X = Br, I) and its Mechanistic Study
   Hitoshi Kuniyasu, Atsushi Sanagawa, Takuya Nakajima, Takanori Iwasaki, Nobuaki Kambe, Karan Bobuatong, and Masahiro Ehara

4. Lewis Acid Catalyzed Intramolecular Fluoroacylation of Alkynes
   Atsushi Sanagawa, Hitoshi Kuniyasu, Takanori Iwasaki, and Nobuaki Kambe
   *in preparation*
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