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ン類の分子内アシルフルオロ化反応に関する研究）

Atsushi Sanagawa

January 2015

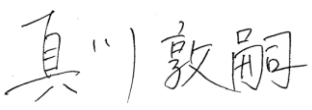
Graduate School of Engineering

Osaka University

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.

Department of Applied Chemistry
Graduate School of Engineering, Osaka University
Suita, Osaka, Japan
January, 2015



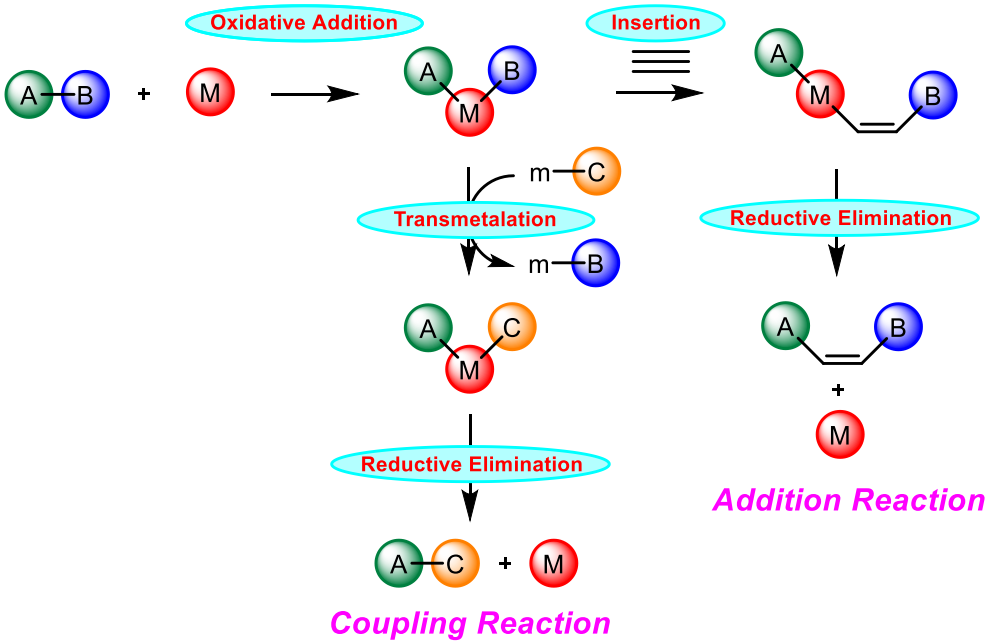
Atsushi Sanagawa

Contents

Chapter 4. Lewis Acid Catalyzed Intramolecular Acylfluorination of Alkynes

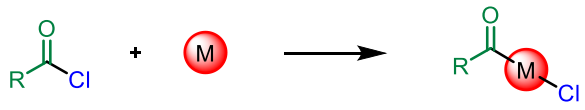
General Introduction

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

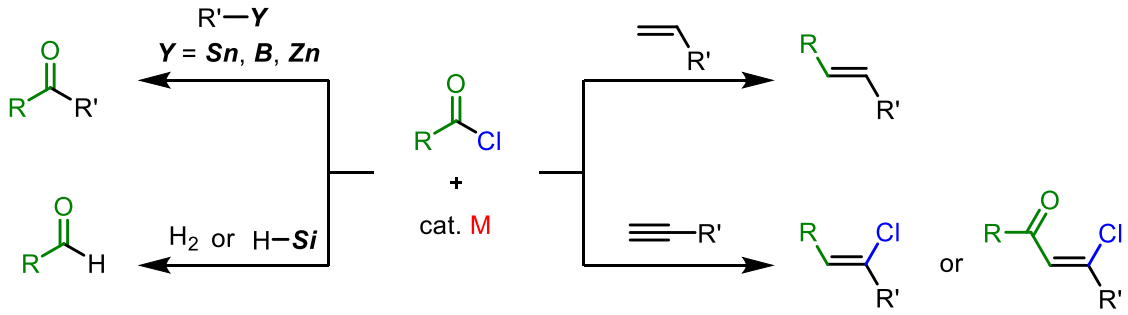


Scheme 1. Transition-metal Catalyzed Reactions Trigged by Oxidative Addition

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. Oxidative Addition of Acid Halides



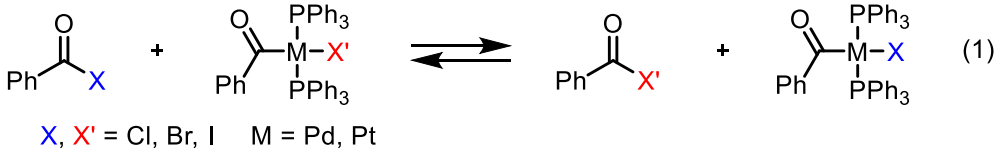
Scheme 3. Transition-Metal Catalyzed Reactions Using Acid Halides

Thioesters (RC(O)-X; X = SR'), acid halides delivertives, 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 reserch 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 iodies 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.

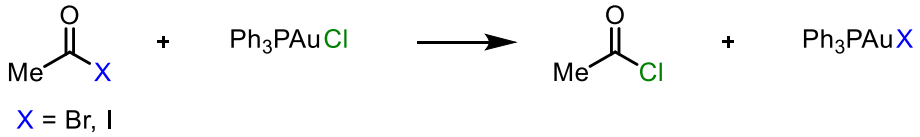
The author launched a study on novel transformations of transition-metal complexes and catalytic reaction utilizing characteristic reactivity of acid halides. The present thesis consists of the halogen-exchange reactions of various transition-metal complexes with acid halides and Lewis acid catalyzed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

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

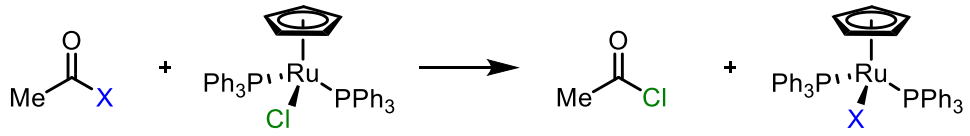


(1)

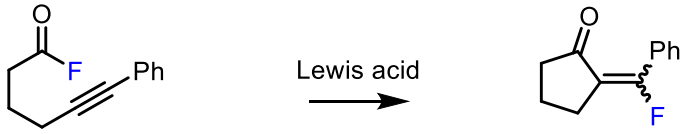
In chapter 2, the halogen exchange reactions between aurous complexes and acid halides are discribed.



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



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



References and Notes

[1] (a) Dent, S. P.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1975**, *97*, 307. (b) Mukhedkar, A. J.; Green, M.; Stone, F. A. *J. Chem. Soc. A* **1970**, *947*. (c) Cook, C. D.; Jauhal, G. S. *Can. J. Chem*. **1967**, *45*, 301. (d) Baird, M. C.; Wilkinson, G. *J. Chem. Soc. A.* **1967**, 865. (e) Cook, C. D.; Jauhal, G. S. *Can. J. Chem.* **1967**, *45*, 301.

[2] For a review; (a) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177.; Stille coupling reactions; (b) Labadie, J. W.; Tueting, D.; Stille, J. K. *J. Org. Chem.* **1983**, *48*, 4634. (c) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129. (d) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *J. Organomet. Chem.* **1985**, *291*, 129. (e) Ye, J.; Bhatt, R. K.; Falck, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 1. (f) Cox, R. J.; Ritson, D. J.; Dane, T. A.; Berge, J.; Charmant, J. P. H.; Kantacha, A. *Chem. Commun.* **2005**, 1037. (g) Thibonnet, J.; Abarbri, M.; Parrain, J.-L.; Duchene, A. *J. Org. Chem.* **2002**, *67*, 3941. (h) Davis, J. L.; Dhawan, R.; Arndtsen, B. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 590. Suzuki coupling reactions; (i) Chen, H.; Deng, M.-Z. *Org. Lett.* **2000**, *2*, 1649. Negishi coupling reactions; (j) Østergaard, N.; Skjaerbaek, N.; Begtrup, M.; Vedso, P. J. *Chem. Soc., Perkin Trans. 1* **2002**, 428.; Direct coupling reactions; (k) Zhao, X. D.; Yu, Z. K. *J. Am. Chem. Soc.* **2008**, *130*, 8136. (l) Kochi, T.; Urano, S.; Seki, H.; Mizushima, E.; Sato, M.; Kakiuchi, F. *J. Am. Chem. Soc.* **2009**, *131*, 2792. (m) Zhao, X. D.; Dimitrijević, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466. (n) Jin, W. W.; Yu, Z. K.; He, W.; Ye, W. J.; Xiao, W.-J. *Org. Lett.* **2009**, *11*, 1317. Reductive coupling reaction; (o) Wu, F.; Lu, W.; Qian, Q.; Ren, Q.; Gong, H. *Org. Lett.* **2012**, *14*, 3044.

[3] Reductions of acid halides; (a) Rosenmund, K. W. *Ber. Dtsch. Chem. Ges.* **1918**, *51*, 585. (b) Mosettig, E.; Mozingo, R. *Org. React.* **1948**, *4*, 362. (c) Lee, K.; Maleczka, R. E. Jr. *Org. Lett.* **2006**, *8*, 1887. (d) Gutsulyak, D. V.; Niknov, G. I. *Adv. Synth. Catal.* **2012**, *354*, 607. (e) Fujihara, T.; Cong, C.; Iwai, T.; Terao, J.; Tsuji, Y. *Synlett.* **2012**, *23*, 2389.

[4] Heck type reaction; (a) Sugihara, T.; Satoh, T.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4672.

[5] Addition reactions to alkynes; (a) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941. (b) Kashiwabara, T.; Kataoka, K.; Hua, R.; Shimada, S.; Tanaka, M. *Org. Lett.* **2005**, *7*, 2241. (c) Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6668. (d) Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2012**, *134*, 1268.

[6] Other selected examples; (a) Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2010**, *132*, 9602. (b) Nagata, T.; Hirano, K.; Satoh, T.; Miura. M. *J. Org. Chem.* **2014**, *79*, 8960. (c) Muraoka, T.; Hiraiwa, E. Abe, M.; Ueno, K. *Tetrahedron Lett.* **2013**, *54*, 4309. (d) Fujihara, T.; Tatsumi, K.; Terao, J.; Tsuji, Y. *Org. Lett.*, **2013**, *15*, 2286. (e) Boersch, C.;

Merkul, E.; Muller, T. J. J. *Angew. Chem., Int. Ed.* **2005**, *50*, 10448.

[7] For reviews, see: (a) Fukuyama, T.; Tokuyama, H. *Aldrichimica Acta* **2004**, *37*, 87. (b) Dubbaka, S. R.; Vogel, P. *Angew. Chem. Int. Ed.* **2005**, *44*, 7674. (c) Seki, M. *Synthesis* **206**, *18*, 2975. (d) Prokopcová, H.; Kappe, C. O. *Angew. Chem. Int. Ed.* **2009**, *48*, 2276. For selected examples, see: (e) Fukuyama, T.; Lin, S.-C.; Li, L. *J. Am. Chem. Soc.* **1990**, *112*, 7050. (f) Kanda, Y.; Fukuyama, T. *J. Am. Chem. Soc.* **1993**, *115*, 8451. (g) Miyazaki, T.; Han-ya, Y.; Tokuyama, H.; Fukuyama, T. *Synlett* **2004**, 477. (h) Kimura, M.; Seki, M. *Tetrahedron Lett.* **2004**, *45*, 3219. (i) Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Fukuyama, T. *Tetrahedron Lett.* **1998**, *39*, 3189. (j) Zeysing, B.; Gosch, C.; Terfort, A. *Org. Lett.* **2000**, *2*, 1843. (k) Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260. (l) Wittenberg, R.; Srogl, J.; Egi, M.; Liebeskind, L. S. *Org. Lett.* **2003**, *5*, 3033. (m) Ikeda, Z, Hirayama, H.; Matsubara, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 8200. (n) Yang, H.; Li, H.; Wittenberg, R.; Egi, M.; Huang, W.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 1132. (o) Ooguri, A.; Ikeda, Z.; Matsubara, S. *Chem. Commun.* **2007**, 4761. (p) Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 15734.

[8] For reviews; (a) Kuniyasu, H. In *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; p 217. (b) Kuniyasu, H.; Kambe, N. *Chem. Lett.* **2006**, *35*, 1320. (c) Kuniyasu, H.; Kurosawa, H. *Chem. Eur. J.* **2002**, *8*, 2660. (d) Kuniyasu, H.; Kambe, N. *J. Synth. Org. Chem. Jpn.* **2009**, *67*, 701. For recent examples, see: (e) Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2005**, *127*, 9706. (f) Yamashita, F.; Kuniyasu, H.; Terao, J.; Kambe, N. *Org. Lett.* **2008**, *10*, 101. (g) Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2008**, *130*, 10504. (h) Toyofuku, M.; Murase, E.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *Org. Lett.* **2008**, *10*, 3957.

[9] Kalow, J. A.; Doyle, A. G. *J. Am. Chem. Soc.* **2010**, 132, 3268.

Chapter 1

Ligand Exchange Reaction of Palladium and Platinum Complexes with Acid Halides

1-1 Introduction

Ligand-exchange reactions are fundamental transformations in organometalic 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(TePh)(Ph)$(PEt_3)_2$ 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]

$$M\text{-}L^1 + L^2 \rightleftharpoons M\text{-}L^2 + L^1 \quad (1)$$

$$M^1\text{-}\boldsymbol{X} + M^2 \rightleftharpoons M^1 + M^2\text{-}\boldsymbol{X} \quad (2)$$

$$M^1\text{-}\boldsymbol{X} + M^2\text{-}R \rightleftharpoons M^1\text{-}R + M^2\text{-}\boldsymbol{X} \quad (3)$$

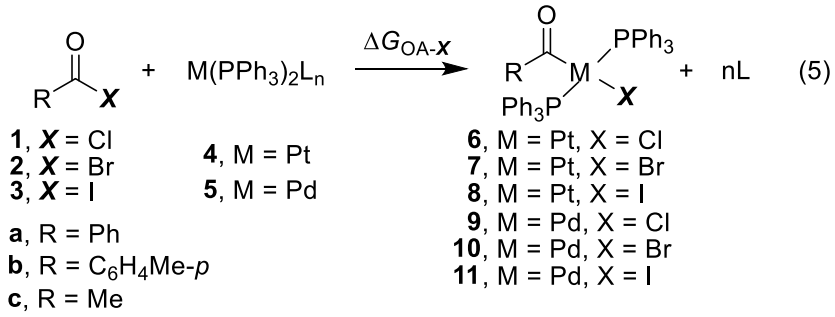
(M^1: transition metal; M^2: typical metal)

$$M\text{-}\boldsymbol{X} + R\text{-}\boldsymbol{X'} \rightleftharpoons M\text{-}\boldsymbol{X'} + R\text{-}\boldsymbol{X} \quad (4)$$

Scheme 1. Representative Reaction Types of Ligand-Exchange Reactions (L: neutral ligand; *X*, *X*': halogen or pseudo halogen)

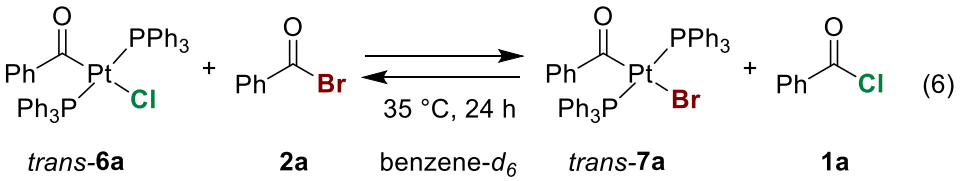
Herein, we wish to demonstrate the following: (1) the utility of such ligand-exchange reactions for determining the relative Δ*G*s of the oxidative addition of acid halides RC(O)*X* (**1**, *X* = Cl; **2**, *X* = Br; **3**, *X* = I) to $M(PPh_3)_2Ln$ (**4**, M = Pt; **5**, M = Pd) producing *trans*-M(X)[C(O)R]$(PPh_3)_2$ (**6**, M = Pt, X = Cl; **7**, M = Pt, X = Br; **8**, M = Pt, X = I; **9**, M = Pd, X = Cl; **10**, M = Pd, X = Br; **11**, M = Pd, X = I) and nL (Eq 5); (2) its reaction mechanism by density functional theory (DFT) method; and (3) synthetic application of the method for the

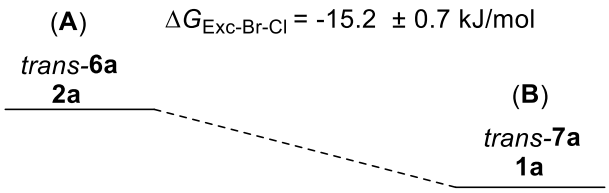
conversion of M-X bonds into M-X' bonds with heavier halogens.



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, δ 20.4, J_{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 °C produced an equilibrium mixture of *trans*-**6a** + **2a** (system **A**) and *trans*-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**7a**) (δ 19.8,J_{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.

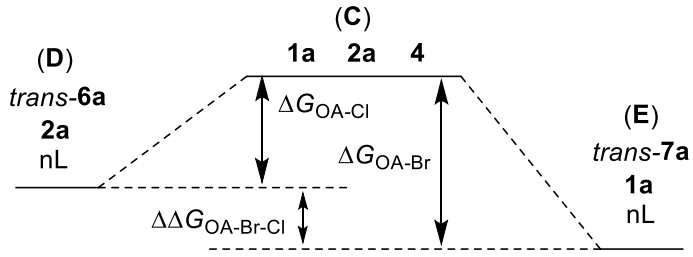




Scheme 2. Δ$G_{Exc-Br-Cl}$ Calculation by the Halogen-Exchange Reaction

By applying the equilibrium constants ***K*** to the equation ΔG = −RTln***K***, the energy gap between **A** and **B** (Δ$G_{Exc-Br-Cl}$) was calculated as −15.2 ± 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$_n$ (**4**) (Scheme 3, **C**), the oxidative addition of **1a** to **4** gives **D** (*trans*-**6a** + **2a** + nL = **A** + nL) with free energy change ΔG_{OA-Cl}, whereas the reaction of **2a** with **4** gives **E** (*trans*-**7a** + **1a** + nL = **B** + nL), accompanied by ΔG_{OA-Br}. Accordingly, Δ$G_{Exc-Br-Cl}$ obtained from Eq 6 is

equal to the free energy gap between $\Delta G_{\text{OA-Br}}$ and $\Delta G_{\text{OA-Cl}}$ ($\Delta G_{\text{Exc-Br-Cl}} = \Delta\Delta G_{\text{OA-Br-Cl}}$).[10,11]



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

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_3)$_2$ (*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_3)$_2$L$_n$ (**4**) producing *trans*-**8a** and nL is −10.9 ± 0.4 kJ/mol ($\Delta\Delta G_{\text{OA-I-Br}}$) more favorable than that of **2a** to **4**, yielding *trans*-**7a** and nL. A similar treatment of *trans*-Pt(Cl)[C(O)Ph](PPh_3)$_2$ (*trans*-**6a**) with PhC(O)I (**3a**) gave both *trans*-Pt(I)[C(O)Ph](PPh_3)$_2$ (*trans*-**8a**) and PhC(O)Cl (**1a**) exclusively within 25 min at 20 °C. Although $\Delta\Delta G_{\text{OA-I-Cl}}$ 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 $\Delta G_{\text{OA-Cl}}$, $\Delta G_{\text{OA-Br}}$, and $\Delta G_{\text{OA-I}}$, respectively. The value of $\Delta\Delta G_{\text{OA-I-Cl}}$ is clearly the gap between **G** and **I**, i.e., the sum of $\Delta\Delta G_{\text{OA-Br-Cl}}$ and $\Delta\Delta G_{\text{OA-I-Br}}$ (-26.1 ± 0.8 kJ/mol).[12,13]

Similarly, the reactions between the corresponding palladium complexes *trans*-Pd(Cl)[C(O)Ph](PPh_3)$_2$ (*trans*-**9a**) and PhC(O)Br (**2a**) afforded the equilibrium mixture of *trans*-**9a** + **2a** and *trans*-Pd(Br)[C(O)Ph](PPh_3)$_2$ (*trans*-**10a**) + **1a** within 60 min at 20 °C: the value of $\Delta\Delta G_{\text{OA-Br-Cl}}$ was −14.6 ± 0.1 kJ/mol. From the reaction of *trans*-**10a** with **3a** producing an equilibrium mixture of *trans*-Pd(Br)[C(O)Ph](PPh_3)$_2$ (*trans*-**10a**) + **3a** and *trans*-Pd(I)[C(O)Ph](PPh_3)$_2$ (*trans*-**11a**) + **2a**, $\Delta\Delta G_{\text{OA-I-Br}}$ was determined to be −6.9 ± 0.1 kJ/mol. Accordingly, $\Delta\Delta G_{\text{OA-I-Cl}}$ was calculated to be −21.5 ± 0.2 kJ/mol. These results are summarized in Tables 1.

Next, $\Delta\Delta G$ valueswere theoretically evaluated using M[C(O)Ph](PH_3)$_2$X as model compounds by DFT calculation with the TPSS functional (Table 1).[14,15] $\Delta\Delta G_{\text{OA-Br-Cl-t}}$(t: theoretical), $\Delta\Delta G_{\text{OA-I-Br-t}}$, and $\Delta\Delta G_{\text{OA-I-Cl-t}}$ 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. $\Delta\Delta G_{\text{OA-Br-Cl-t}}$, $\Delta\Delta G_{\text{OA-I-Br-t}}$, and $\Delta\Delta G_{\text{OA-I-Cl-t}}$ were −20.5, −13.0, and −33.5 kJ/mol, respectively. These results demonstrate that $\Delta\Delta G$ obtained

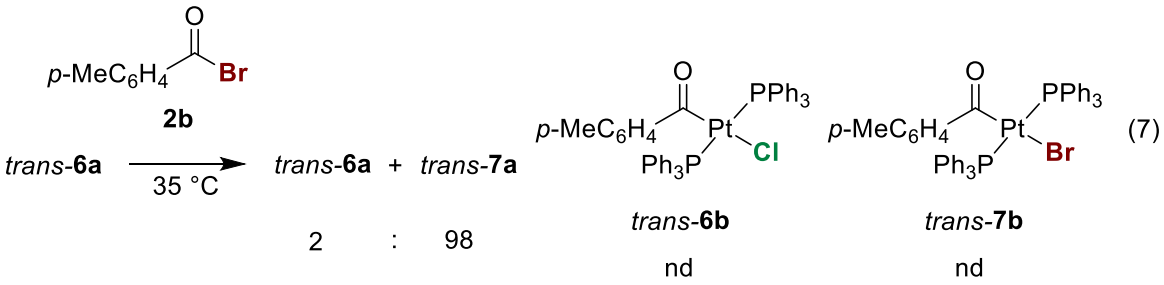
from the experiment are relatively consistent with those of the theoretical calculation, indicating the reliability of the $\Delta\Delta G$ calculation.

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

		M = Pt		M = Pd	
X′	***X***	Exptl $\Delta\Delta G_{\text{OA-}X'\text{-}X}$	Theor $\Delta\Delta G_{\text{OA-}X'\text{-}X\text{-}t}$	Exptl $\Delta\Delta G_{\text{OA-}X'\text{-}X}$	Theor $\Delta\Delta G_{\text{OA-}X'\text{-}X\text{-}t}$
Br	Cl	−15.2 ± 0.7	−17.3	−14.6 ± 0.1	−20.5
I	Br	−10.9 ± 0.4	−11.5	−6.9 ± 0.1	−13.0
I	Cl	−26.1 ± 0.8	−28.9	−21.5 ± 0.2	−33.5

[a]Model systems; M[C(O)Ph](PH$_3$)$_2$X + PhC(O)X' → M[C(O)Ph](PH$_3$)$_2$X' + 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.

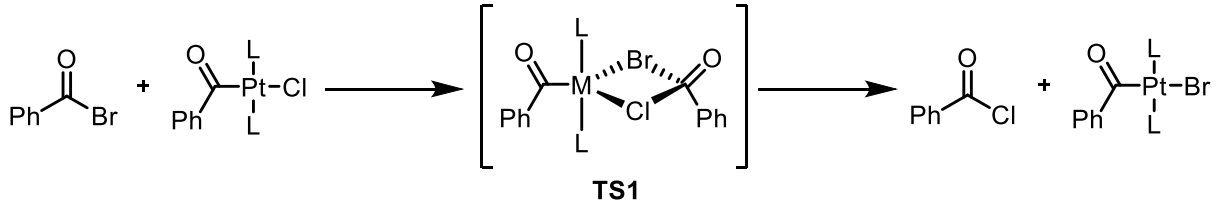
To gain insight into the mechanism of the present halogen-exchange, the reaction of *trans*-Pt(Cl)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**6a**) with *p*-MeC$_6$H$_4$C(O)Br (**2b**) was examined (Eq 7). The reaction selectively afforded a mixture of *trans*-**6a** and *trans*-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**7a**) 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-2**) provides *trans*-Pt(Br)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**7a-1**) and PhC(O)Cl (**1a-2**).[16,17]



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_2Cl_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 PPh_3, TEMPO, or galvinoxyl, which suggests that participation of both a cationic complex $\{Pt[C(O)Ph](PPh_3)_3\}^+X^-$ 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 $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were successfully measured to be 44 ± 3 and –148 ± 9 J/Kmol, respectively.

Next, the mechanism of the σ-bond metathesis shown in Scheme 4 were theoretically examined with the M06 functional.[18] 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 σ-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 $\Delta H^{\ddagger}$ obtained from the experimental data. Moreover, the value of $\Delta S^{\ddagger}$ 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 σ-bond metathesis.* The C=O bond length of C^2 of **TS1** is 1.185 Å, which is barely different from that of free **2a-2** and **1a-2** (1.190 Å).

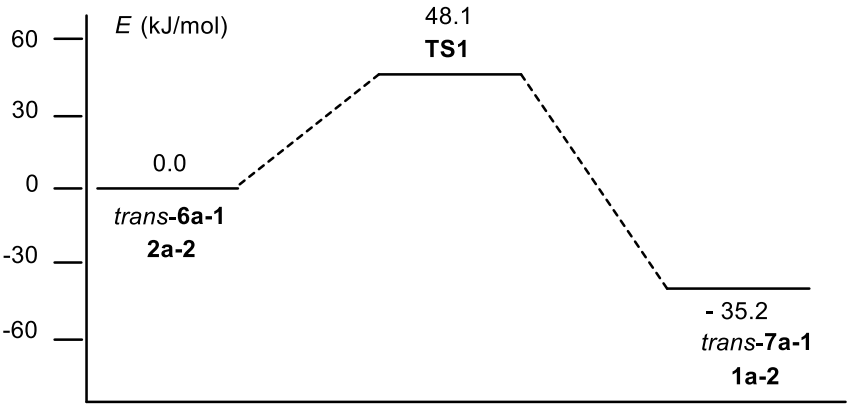


Figure 1. Reaction coordinate of pentaoordinated σ-bond metathesis from *trans*-**6a-1**

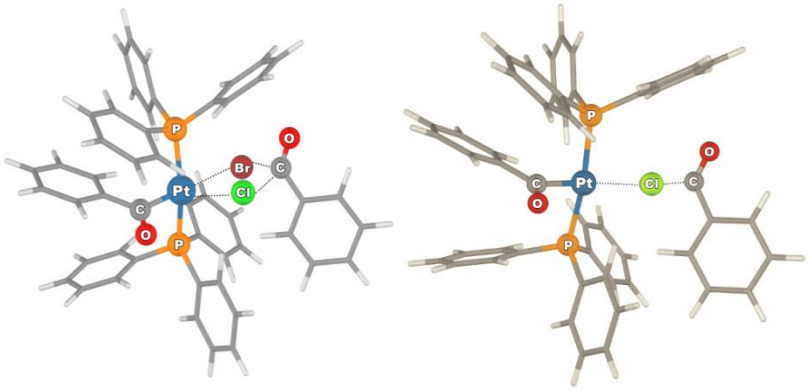


Figure 2. Structure of **TS1** of the Pt-complex via pentacoordinated σ-bond metathesis from *trans*-**6a-1** (two different views).

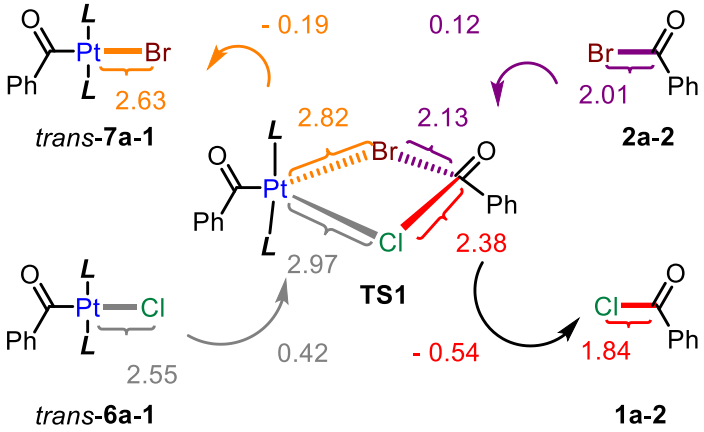


Figure 3. Selected bond distances (Å) of the optimized structures of reactants, **TS1** and products.

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**.

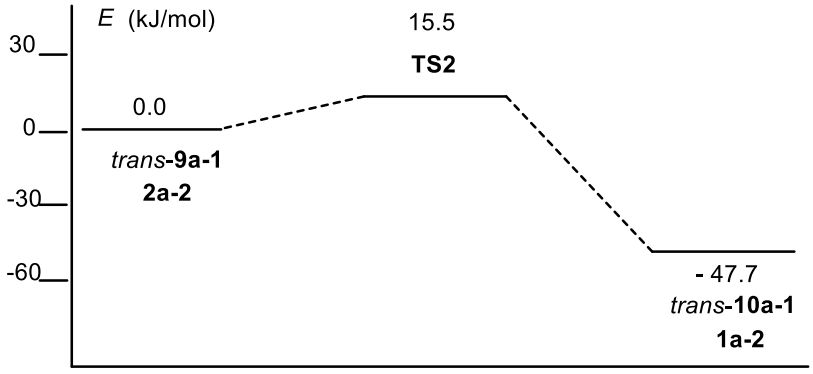


Figure 4. Reaction coordinate of pentacoordinated σ-bond metathesis from *trans*-**9a-1**.

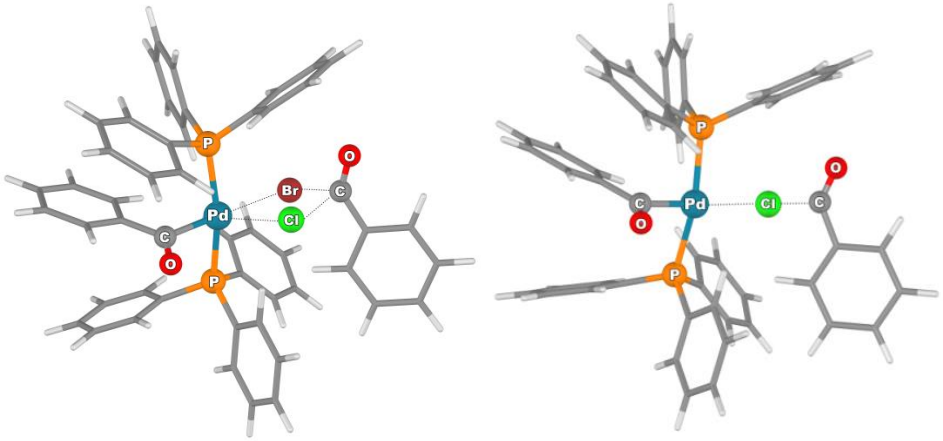


Figure 5. Structure of **TS2** of the Pd-complex formed from *trans*-**9a-1** via pentacoordinated σ-bond metathesis (two different views).

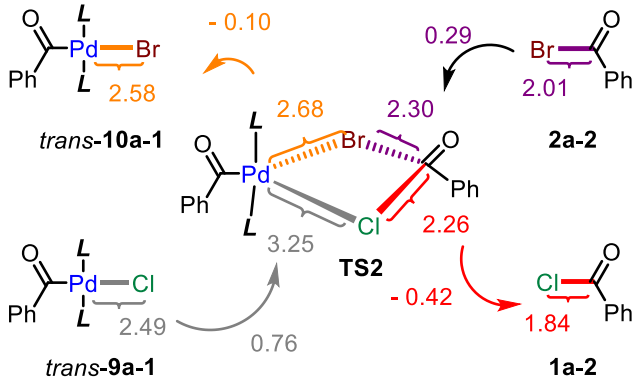
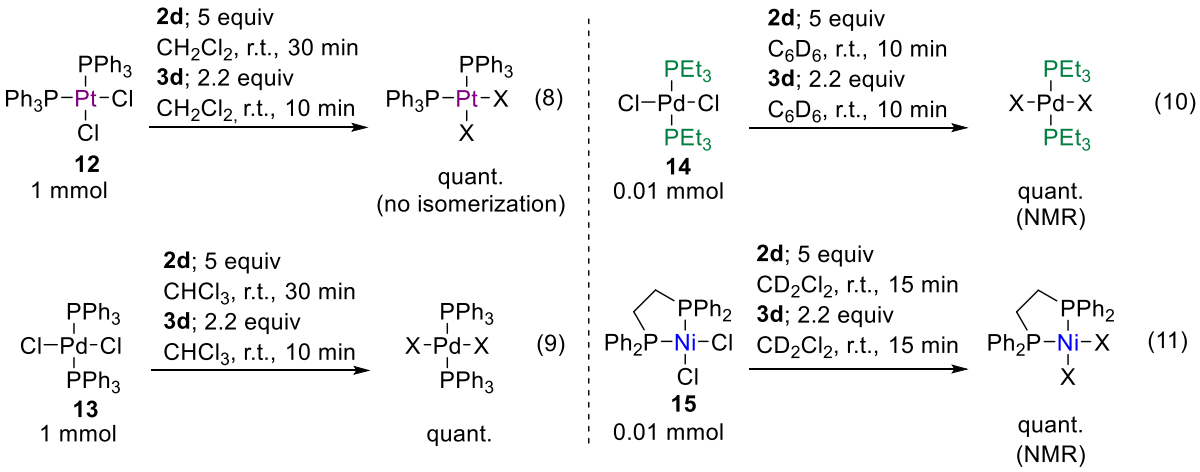


Figure 6. Selected bond distances (Å) of the optimized structures of reactants, **TS2** and products.

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** (2.58Å) 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](PPh$_3$)$_2$ 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)$_2$(PPh$_3$)$_2$] (**12**) with 4.0-mmol MeC(O)(Br) (**2c**) in CH_2Cl_2 (50 mL) at 20 °C for 30 min, the solvent, excess **2c** (b.p. 75 °C–77 °C), and byproduct of MeC(O)(Cl) (**1c**) (b.p. 52 °C) were removed by subjecting the reaction mixture under reduced pressure to produce the analytically pure *cis*-[Pt(Br)$_2$(PPh$_3$)$_2$] quantitatively (Eq 8).[19] 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.[20] Moreover, the corresponding iodide was isolated similarly by the treatment of **12** with $CH_3C(O)I$ (**3c**, b.p. 108 °C) and subsequent evaporation. Similarly, the reaction of *trans*-[Pd(Cl)$_2$(PPh$_3$)$_2$] (**13**) with **2c** and **3c** afforded *trans*-[Pd(Br)$_2$(PPh$_3$)$_2$] and *trans*-[Pd(I)$_2$(PPh$_3$)$_2$], respectively (Eq 9).[21] 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)$_2$(PEt$_3$)$_2$] (**14**) and [Ni(Cl)$_2$(dppe)] (**15**) into *trans*-[Pd(***X***)$_2$(PEt$_3$)$_2$] and [Ni(***X***)$_2$(dppe)] (***X*** = Br and I) were facilely achieved (Eq 10 and

11).[22,23]



1-3 Conclusions

The significance of the present study is summarized as follows: (1) the reactions of *trans*-M(***X***)[C(O)R](PPh$_3$) with RC(O)***X'*** produced clean equilibrium mixtures of *trans*-M(***X***)[C(O)R](PPh$_3$)/RC(O)***X'*** and *trans*-M(***X'***)[C(O)R](PPh$_3$)/RC(O)***X***; (2) ΔG values were equal to the relative ΔGs of the oxidative additions of RC(O)***X***/ RC(O)***X'*** to M(PPh$_3$)$_2$L$_n$, which was clearly supported by DFT calculation; (3) both experimental and computational studies substantiated that the reaction occurred via pentacoordinated σ-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}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% H$_3$PO$_4$ (aq) as an external standard, and S=P(C$_6$H$_4$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*-MeC$_6$H$_4$C(O)Cl (**1c**), and MeC(O)Cl (**1d**) were commercially obtained.. *p*-MeC$_6$H$_4$C(O)Br (**2b**) and *p*-MeC$_6$H$_4$C(O)I (**3b**) were synthesized by the reaction of **1c** with Me$_3$SiBr and Me$_3$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 *trans*-M(***X***)[C(O)R](PPh$_3$)$_2$ (**6**, M = Pt, ***X*** = Cl; **7**, M = Pt, ***X*** = Br; **8**, M = Pt, ***X*** = I; **9**, M = Pd, ***X*** = Cl; **10**, M = Pd, ***X*** = Br; **11**, M = Pd, ***X*** = I) were prepared by the

reaction of $Pt(PPh_3)_2(C_2H_4)$ 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_6D_6) δ 20.4 (J_{Pt-P} = 3360 Hz).
trans-**7a:** ^{31}P NMR (161 MHz, C_6D_6) δ 19.8 (J_{Pt-P} = 3340 Hz).
trans-**8a:** ^{31}P NMR (161 MHz, C_6D_6) δ 17.5 (J_{Pt-P} = 3300 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_2O 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_6D_6) δ 6.74 (t, *J* = 7.3 Hz, 2 H), 6.83 (t, *J* = 7.3 Hz, 1 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_6D_6) δ 19.22 (s); Anal. Calcld for $C_{43}H_{35}ClOP_2Pd$: 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_6D_6) δ 6.76 (t, *J* = 7.3 Hz, 2 H), 6.84 (t, *J* = 7.2 Hz, 1 H), 6.93-6.95 (m, 18 H), 7.92-7.97 (m, 14 H); IR (KBr) 3053, 1650, 1481, 1435, 1183, 1149, 871, 743, 691, 633 cm^{-1}; ^{31}P NMR (161 MHz, C_6D_6) δ 19.22 (s); Anal. Calcld for $C_{43}H_{35}BrOP_2Pd$: 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_6D_6) δ 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, 1148, 868, 742, 690, 628 cm^{-1}; ^{31}P NMR (161 MHz, C_6D_6) δ 19.18 (s); Anal. Calcld for $C_{43}H_{35}IOP_2Pd$: C, 59.84; H, 4.09. Found: C, 60.12; H, 4.00.

All the reaction samples descried 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_6H_4OMe-*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 *trnas*-**7a** + **1a**. Neither *cis*-**6a** nor *cis*-**7a** was detected during the course of the reaction. The equilibrium constant K = [**1a**][*trans*-**7a**]/[**2a**][*trans*-**6a**] was calculated to be 2.5 x 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 ± 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 $Pt(PPh_3)_2(C_2H_4)$ 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 ± 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 ± 0.8 kJ/mol as a sum of $\Delta\Delta G_{\text{EXC-Br-Cl}}$ and $\Delta\Delta G_{\text{EXC-I-Br}}$ 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 $S{=}P(C_6H_4OMe\text{-}p)_3$ (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 ± 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 $\Delta G_{\text{OA-Br-I}}$ was calculated to be -6.9 ± 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 ± 0.2 kJ/mol as a sum of $\Delta\Delta G_{\text{EXC-Br-Cl}}$ and $\Delta\Delta G_{\text{EXC-I-Br}}$.

Halogen Exchange Reaction between *trans*-6a and *p*-MeC$_6$H$_4$C(O)Br (2b)

Into a dry Pyrex NMR tube were added *trans*-**6a** (8.4 mg, 0.0098 mmol), *p*-MeC$_6$H$_5$C(O)Br (**2c**, 2.4 mg, 0.012 mmol), S=P(C$_6$H$_4$OMe-*p*)$_3$ (1.2 mg, 0.0031 mmol) and benzene-*d*$_6$ (0.5 mL). The reaction at 35 °C was monitored by ^{31}P and ^{1}H 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)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**6b**) nor Pt(Br)[C(O)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**7b**) was detected. On the other hand, the reaction of *trans*-Pt(Cl)[C(O)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**6b**) with PhC(O)Br (**2a**) produced *trans*-Pt(Br)[C(O)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**7b**). However, neither *trans*-**6a** nor *trans*-**7a** was detected.

trans-**6c:** ^{31}P NMR (161 MHz, C$_6$D$_6$) δ 18.9 (J_{Pt-P} = 3408 Hz) (data collected by the reaction of **1c** with Pt(PPh$_3$)$_2$(C$_2$H$_4$))

trans-**7c:** ^{31}P NMR (161 MHz, C$_6$D$_6$) δ 18.2 (J_{Pt-P} = 3387 Hz) (data collected by the reaction of **2c** with Pt(PPh$_3$)$_2$(C$_2$H$_4$) (**4a**))

Similarly, the reaction of *trans*-Pd(Cl)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**9a**) with **2b** selectively produced *trans*-Pd(Br)[C(O)Ph](PPh$_3$)$_2$ (*trans*-**10a**). Neither formation of *trans*-Pd(Cl)[C(O)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**9b**) nor *trans*-Pd(Br)[C(O)C$_6$H$_4$Me-*p*](PPh$_3$)$_2$ (*trans*-**10c**) was confirmed.

trans-**9c:** ^{31}P NMR (161 MHz, C$_6$D$_6$) δ 19.3 (data collected by the reaction of **1b** with Pd(PPh$_3$)$_4$)

trans-**10c:** ^{31}P NMR (161 MHz, C$_6$D$_6$) δ 19.6 (data collected by the reaction of **2b** with Pd(PPh$_3$)$_4$)

Halogen Exchange Reaction in the Presence of Free PPh$_3$

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), PPh$_3$ (0.3 mg, 10 mol%), S=P(C$_6$H$_4$OMe-*p*)$_3$ (1.9 mg, 0.0050 mmol) and benzene-*d*$_6$ (0.5 mL). The reaction at 35 °C was monitored by ^{31}P and ^{1}H NMR spectroscopies. However, the reaction rate was not affected by the addition of PPh$_3$. The reaction of *trans*-**6a** with **2a** performed in CD$_2$Cl$_2$ also took place with a similar reaction rate to the reaction carried out in C$_6$D$_6$.

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(C$_6$H$_4$OMe-*p*)$_3$ (1.9 mg, 0.0050 mmol) and benzene-*d*$_6$ (0.5 mL) with the sample cooled by dry ice/*i*-PrOH bath. Then the reaction was monitored at -40 °C by ^{31}P 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 toluende-d_8 according to the equation $k = (k_B T/h)\{\exp[-(\Delta H^{\ddagger} - T\Delta S^{\ddagger})/(RT)]\}$. Reaction temperature and reaction rates (k_{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)[C(O)Ph](PPh$_3$)$_2$ (*trans*-6a) and Br of MeC(O)Br (2d):

Into a dry Pyrex NMR tube were added S=P(C_6H_4OMe-*p*)$_3$ (1.9 mg, as an internal standard), *trans*-**6a** (**8.6** mg, 0.010 mmol), and benzene-d_6 (0.5 mL). After the sensitivity of *trans*-**6a** to the internal standard was measured by ^{31}P NMR spectrum, MeC(O)Br (**2d**, 4.9 mg, 0.040 mmol) was added. Then, the reaction at 25 °C was monitored by ^{31}P and ^{1}H 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)$_2$(PPh$_3$)$_2$ (**12**, 701.9 mg, 1.0 mmol) and CH_2Cl_2 (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, CH_2Cl_2, **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)$_2$(PPh$_3$)$_2$ (870 mg) quantitatively. The corresponding iodide *cis*-Pt(I)$_2$(PPh$_3$)$_2$ was also isolated similarly with the treatment of **12** with $CH_3C(O)I$ (**3c**). Similarly, the Cl atoms of *trans*-Pd(Cl)$_2$(PPh$_3$)$_2$, trans-Pd(Cl)$_2$(PEt$_3$)$_2$, 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 $\Delta G_{OA\text{-}X\text{-}t}$ of Platinum Complexes with TPSS Functiona

The Gibbs free energies (*G*) of the reactants and products in the reactions of PhC(O)***X*** + $Pt(PH_3)_2(C_2H_4)$ (**4a'**) → *trans*-Pt(***X***)[C(O)Ph]$(PH_3)_2$ + C_2H_4 (***X*** = Cl, Br, and I) are shown in Table S1. The $\Delta G_{OA\text{-}X}$ and $\Delta\Delta G_{OA\text{-}X\text{-}X'}$ 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).

Compound	G (a.u.)
$Pt(PH_3)_2(C_2H_4)$ (**4a'**)	-884.3494
C_2H_4	-78.5760
trans-Pt(Cl)[C(O)Ph]$(PH_3)_2$ (**6a'**)	-1611.0106
PhC(O)Cl (**1a**)	-805.2226
trans-Pt(Br)[PhC(O)]$(PH_3)_2$ (**7a'**)	-3724.8480
PhC(O)Br (**2a**)	-2919.0534
trans-Pt(I)[PhC(O)]$(PH_3)_2$ (**8a'**)	-1448.3853
PhC(O)I (**3a**)	-642.5863

Table S2. $\Delta G_{OA\text{-}X}$ and $\Delta\Delta G_{X\text{-}X'}$ by Experiment in C_6D_6 and Theoretical Calculation in Gas Phase (kJ/mol).

	$\Delta G_{OA\text{-}Cl}$	$\Delta G_{OA\text{-}Br}$	$\Delta G_{OA\text{-}I}$	$\Delta\Delta G_{Cl\text{-}Br}$	$\Delta\Delta G_{Br\text{-}I}$	$\Delta\Delta G_{Cl\text{-}I}$
Expt.	-	-	-	-15.2±0.7	-10.9±0.4	-26.1±0.8
Theory	-38.33	-55.66	-67.21	-17.3	-11.5	-28.9

1-2. Calculation of $\Delta G_{OA\text{-}X\text{-}t}$ 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*** +

$Pd(PH_3)_2(C_2H_4)$ (**4a'**) → *trans*-Pd(***X***)[C(O)Ph]$(PH_3)_2$ + C_2H_4 (***X*** = Cl, Br, and I) are shown in Table S3. The Δ*G* and ΔΔ*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).

Compound	G (a.u.)
$Pd(PH_3)_2(C_2H_4)$ (**4a'**)	-892.8445
C_2H_4	-78.5679
trans-Pd(Cl)[C(O)Ph]$(PH_3)_2$ (**9a'**)	-1619.4627
PhC(O)Cl (**1a**)	-805.1801
trans-Pd(Br)[PhC(O)]$(PH_3)_2$ (**10a'**)	-3733.3143
PhC(O)Br (**2a**)	-2919.0239
trans-Pd(I)[PhC(O)]$(PH_3)_2$ (**11a'**)	-1456.8636
PhC(O)I (**3a**)	-642.5863

Table S4. $\Delta G_{OA\text{-}X}$ and $\Delta\Delta G_{X\text{-}X'}$ by Experiment in C_6D_6 and Theoretical Calculation in Gas Phase (kJ/mol).

	$\Delta G_{OA\text{-}Cl}$	$\Delta G_{OA\text{-}Br}$	$\Delta G_{OA\text{-}I}$	$\Delta\Delta G_{Cl\text{-}Br}$	$\Delta\Delta G_{Br\text{-}I}$	$\Delta\Delta G_{Cl\text{-}I}$
Expt.	-	-	-	-14.6±0.1	-6.9±0.1	-21.5±0.2
Theory	-15.70	-36.24	-49.23	-20.54	-12.99	-33.53

Reaction Mechanisms through σ-Bond Metatheses

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

	trans-**6a-1**	**TS1**	*trans*-**7a-1**	**1a**	**2a**
$R_{Pt\text{-}Br}$	-	2.823	2.633	-	-
$R_{Pt\text{-}Cl}$	2.548	2.967	-	-	-
$R_{C\text{-}Br}$	-	2.125	-	-	2.007
$R_{C\text{-}Cl}$	-	2.384	-	1.840	-
$R_{C\text{-}O}$	1.221	1.185	1.221	1.190	1.190

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**.

	trans-**9a**	**TS2**	*trans*-**10a**	**1a**	**2a**
$R_{Pd\text{-}Br}$	-	2.683	2.578	-	-
$R_{Pd\text{-}Cl}$	2.492	3.250	-	-	-
$R_{C\text{-}Br}$	-	2.301	-	-	2.007
$R_{C\text{-}Cl}$	-	2.262	-	1.840	-
$R_{C\text{-}O}$	1.215	1.180	1.215	1.190	1.190

Table S7. The Calculated Total Energies (*E*) and Energy Including Zero-point Energy Correction (E_{zero}) of the Reactants, Transition States, Intermediates, and Products.

Compound	*E* (a.u.)	E_{zero} (a.u.)
trans-**6a-1**	-2991.745438	-2991.055633
2a-2	-2915.735812	-2915.630838
1a-2	-804.358833	-804.253195
trans-**7a-1**	-5103.135818	-5102.446027
TS1	-5907.462865	-5906.667600
***trans*-9a-1**	-2999.339544	-2998.650837
TS2	-5915.069470	-5914.273901
***trans*-10a-1**	-5110.728794	-5110.040764

3-5 References and Notes

[1] (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Book: Mill Valley, 1987. (b) Tsuji, J. *Transition Metal Reagents and Catalysts*; Wiley, 2000. (c) Rode, B. M.; Schwenk, C. F.; Hofer, T. S.; Randlf, B. R. *Coord. Chem. Rev.* **2005**, *249*, 2993. (d) Stille, J. K.; Lau, K. *Acc. Chem. Res.* **1977**, *10*, 434.

[2] For example: (a) Eeaini, S.; Deacon, G. B.; Hilder, M.; Junk, P. C.; Turner, D. R. *Eur. J. Inorg. Chem.* **2006**, *17*, 3434. (b) Deacon, G. B.; Fallon, G. D.; Forsyth, C. M.; Harris, S. C.; Junk, P. C.; Skelton, B. W.; White, A. H. *Dalton Trans.* **2006**, 802. (c) Vcente, J.; Arcas, A.; Fernandez-Hernandez, Jesus, M.; Sironi, A.; Masciocchi, N. *Chem. Commun.* **2005**, 1267. (d) Banerjee, M.; Roy, S. *Chem. Commun.* **2003**, 534.¥

[3] Metal-catalyzed Cross-coupling Reactions; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998.

[4] (a) Han, L.; Choi, N.; Tanaka, M. *J. Am. Chem. Soc.* **1997**, *119*, 1795. (b) Osakada, K.; Maeda, M.; Nakamura, Y.; Yamamoto, T.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 442. (c) Martinezí-Prieto, L. M.; Melero, C.; Río, D.; Palma, P.; Cámpora, J.; Álvarez, E. *Organometallics* **2012**, *31*, 1425. (d) Yamamoto, T.; Kohara, T.; Osakada, K.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2147. (e) Yamamoto, T.; Kohara, T.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2010.

[5] For reviews: (a) Kuniyasu, H. In *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, 2001; 217. (b) Kuniyasu, H.; Kambe, N. *Chem. Lett.* **2006**, *35*, 1320. (c) Kuniyasu, H.; Kurosawa, H. *Chem. Eur. J.* **2002**, *8*, 2660. (d) Kuniyasu, H.; Kambe, N. *J. Synth. Org. Chem. Jpn.* **2009**, *67*, 701.

[6] Minami, Y.; Kuniyasu, H.; Terao, J.; Kambe, N. *Organometallics* **2006**, *24*, 2949.

[7] Kato, T.; Kuniyasu, H.; Kajiura, T.; Minami, Y.; Ohtaka, A.; Kinomoto, M.; Terao, J.; Kurosawa, H.; Kambe, N. *Chem. Commun*. **2006**, 868.

[8] (a) Sugoh, K.; Kuniyasu, H.; Sugae, T.; Ohtaka, A.; Takai, Y.; Tanaka, A.; Machino, C.; Kambe, N.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 5108. (b) Hirai, T.; Kuniyasu, H.; Kato, T.; Kurata, Y.; Kambe, N. *Org. Lett.* **2003**, *5*, 3871. (c) Hirai, T.; Kuniyasu, H.; Kambe, N. *Chem. Lett.* **2004**, *33*, 1148. (d) Hirai, T.; Kuniyasu, H.; Asano, S.; Terao, J.; Kambe, N. *Synlett* **2005**, 1161. (e) Toyofuku, M.; Fijiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2005**, *127*, 9706. (f) Yamashita, F.; Kuniyasu, H.; Terao, J.; Kambe, N. *Org. Lett.* **2008**, *10*, 101. (g) Toyofuku, M.; Murase, E.; Fujiwara, S.; Shin-ike T.; Kuniyasu, H.; Kambe, N. *Org. Lett.* **2008**, *10*, 3957. (h) Minami, Y.; Kuniyasu, H.; Kambe, N. *Org. Lett.* **2008**, *10*, 2469. (i) Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2008**, *130*, 10504. (j) Toyofuku, M.; Murase, E.; Nagai, H.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *Eur. J. Org. Chem.* **2009**, 3141. (k) Minami, Y.; Kuniyasu, H.; Miyafuji, K.; Kambe, M. *Chem. Commun.* **2009**, 3080. (l) Fujiwara, S.; Toyofuku, M.; Kuniyasu, H.; Kambe, N. *Pure Appl. Chem.* **2010**, *82*, 565.

[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.

[10] The oxidative additions of acid halides to $Pt(PPh_3)_n$ have been well-documented. See: (a) Cook, C. D.; Jauhal, G. S. *Can. J. Chem.* **1967**, *45*, 301. (b) Baird, M. C.; Wilkinson, G. *J. Chem. Soc. A.* **1967**, 865. (c) Mukhedkar, A. J.; Green, M.; Stone, F. G. A.; *J. Chem. Soc. A* **1969**, 3023. (d) Mukhedkar, A. J.; Green, M.; Stone, F. A. *J. Am. Chem. A* **1970**, 947. (e) Dent, S. P.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1975**, *97*, 307.

[11] For catalytic reactions triggered by the oxidative addition of acid halides to low-valent transition-metal complexes, see: (a) Iwai, T.; Fujiwara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem.*

Soc. **2010**, *132*, 9602. (b) Iwai, T.; Fujiwara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6668. (c) Zhao, X.; Yu, Z. *J. Am. Chem. Soc.* **2008**, *130*, 8136. (d) Kashiwabara, T.; Fuse, K.; Hua, R.; Tanaka, M. *Org. Lett.* **2008**, *10*, 5469. (e) Kashiwabara, T.; Kataoka, K.; Hua, R.; Shimada, S.; Tanaka, M. *Org. Lett.* **2005**, *7*, 2241. (f) Sugihara, T.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4672. (g) Obora, Y.; Tsuji, Y.; Kawamura, T. *J. Am. Chem. Soc.* **1995**, *117*, 9814. (h) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 1995.

[12] Because the reactions of **1a**, **2a**, and **3a** with $Pt(PPh_3)_2(C_2H_4)$ (**4a**) and $Pt(PPh_3)_4$ (**4b**) both quantitatively produce *trans*-**6a**, *trans*-**7a**, and *trans*-**8a**, respectively, nL can be either C_2H_4 or $2PPh_3$.

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

[14] (a) Frisch, M. J. et al. GAUSSIAN09, Revision B.01; Gaussian, Inc.: Wallingford, CT, **2010**. (b) Tao, J.M.; Perdew, J. P.; Staroerov, V. N.; Scuseria, G. E. *Phys. Rev. Lett.* **2003**, *91*, 146401.

[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_6H_4Me-*p*]$(PPh_3)_2$ (*trans*-**6c**) with PhC(O)Br (**2a**) produced *trans*-Pt(Br)[C(O)C_6H_4Me-*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*-$MeC_6H_4C(O)Br$ (**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.

[19] Rigamonti, L.; Forani, A.; Manassero, M.; Manassero, C.; Pasini, A. *Inorg. Chem.* **2010**, *49*, 123.

[20] For example: (a) Nawara, A.; Shima, T.; Hampel, F.; Gladysz, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 4962. (b) Baber, R. A.; Haddow, M. F.; Middleton, A. J.; Orpen, A. G.; Pringle, P. G.; Haynes, A.; Williams, G. L.; Papp, R. *Organometallics* **2007**, *26*, 713. (c) Brunker, T. J.; Blank, N. F.; Moncar, J. R.; Scriban, C.; Anderson, B. J.; Glueck, D. S.; Zakharov, L. N.; Golen, J. A.; Sommer, R. D.; Incarvito, C. D.; Rheingold, A. L. *Organometallics*, **2005**, *24*, 2730. (d) Suzuki, T.; Kita, M.; Kashiwabara, K.; Fujita, J. *Bull.Chem. Soc. Jpn.* **1990**, *63*, 3434. (e) Higgins, S.; Taylor, R.; Shaw, B. *J. Organomet. Chem.* **1987**, *325*. 285.

[21] Amatore, C.; Jutand, A.; Mottier, L. *Eur. J. Inorg. Chem.* **1999**, 1081.

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

Organometallics, **2002**, *21*, 5373. (b) Jun, H.; Young, V. G.; Angelici, R. J. *Organomtallics*, **1994**, *13*, 2444. (c) Mednikov, E. G.; Dahl, L. F. *Inorg. Chim. Acta*. **2005**, *385*, 1557.

[23] Jarrett, P. S.; Sadler, P. *J. Inorg. Chem.* **1991**, *30*, 2098.

Chapter 2

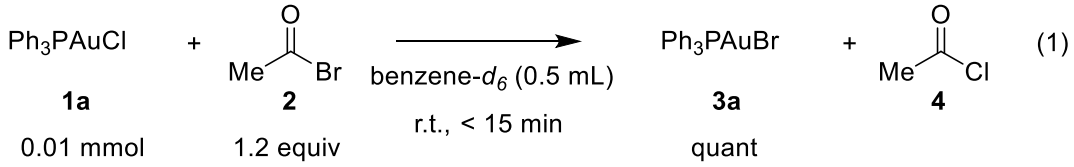
Ligand Exchange Reaction of Aurous Complexes with Acid Halides

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 Li***X***, K***X***, and Na***X*** (***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, dryness with desiccant, and recrystallization are required to obtain analytically pure products. On the other hand, we have demonstrated in Capter 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_3PAuCl (**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** (δ 33.4) was quantitatively converted into Ph_3PAuBr (**3a**) (δ 35.2) (Eq. 1).



In Chapter 1, we succeeded in demonstrating that the Cl-to-Br ligand exchange reaction between *trans*-M(Cl)[C(O)Ph]$(PPh_3)_2$ (M = Pt and Pd) and PhC(O)Br took place through σ-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 σ-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**.

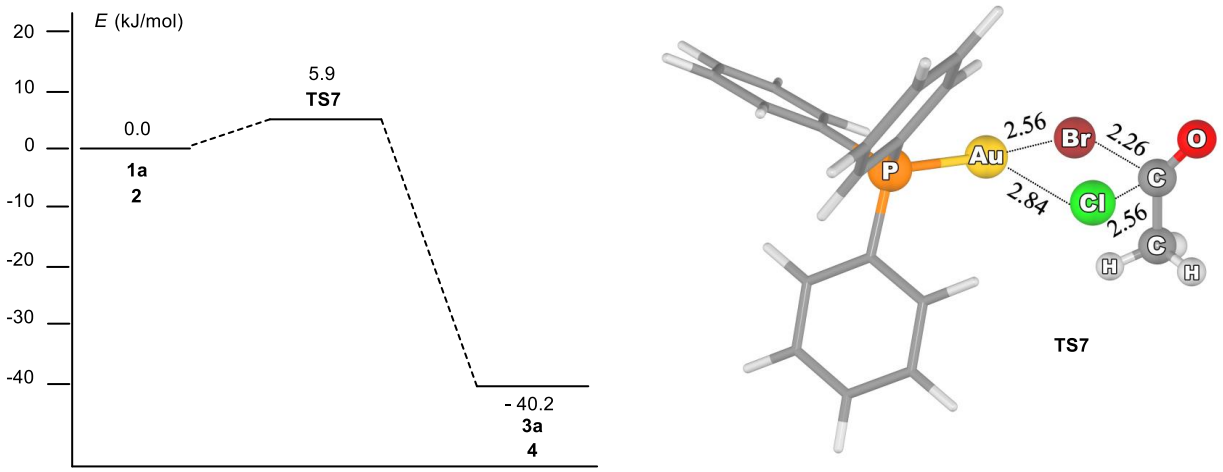


Figure 1. The energy diagram of the reaction of **1a** with **2** *via* tricoordinated σ-bond metathesis and Structure of **TS7** by DFT study with M06 functional.

The dihedral angle of ∠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.

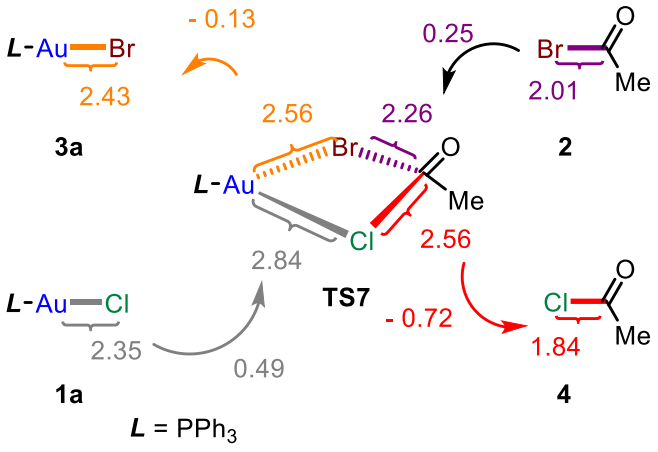


Figure 2. The selected bond lengths (Å) of starting materials, products, and **TS7.**

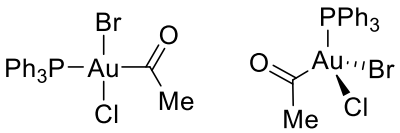


Figure 3. The possible Au(III) complexes.

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).[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**.

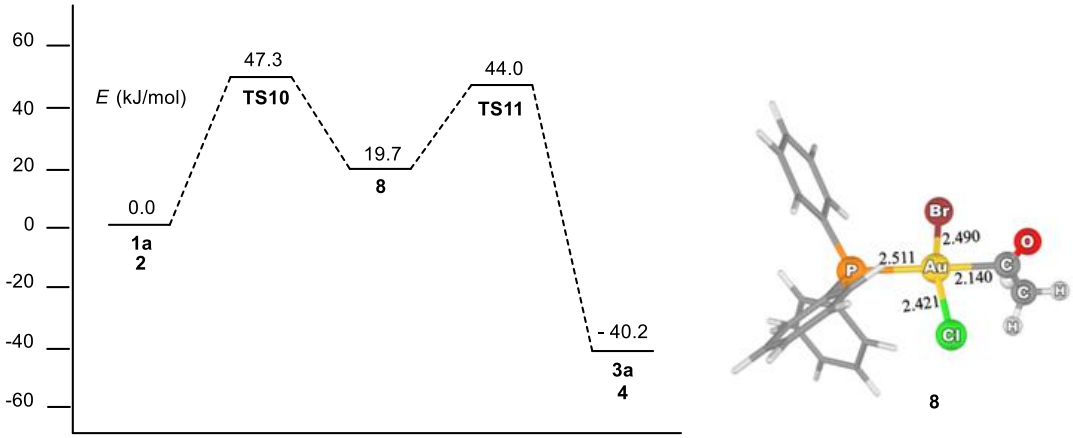
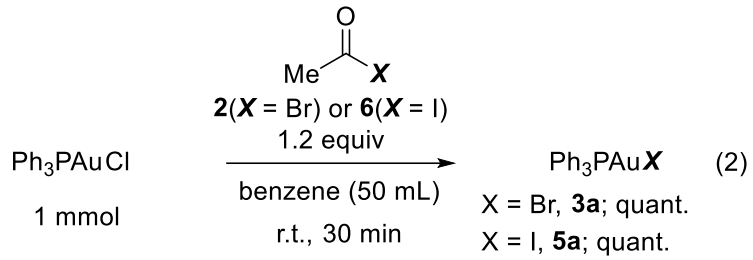


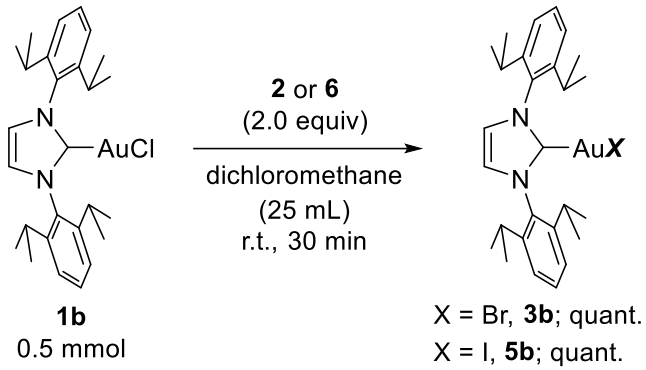
Figure 4. Calculated energy profile of the halogen exchange reaction between Au(Cl)(PPh_3) (**1a**) and MeC(O)Br (**2**)*via* square planar Au(III) complex (**8**).

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 C_6H_6 (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 $CH_3C(O)Cl$ (**4**, b.p. 52 °C) were removed in vacuo. The ^{31}P and ^{1}H NMR spectra as well as elemental analysis of the product demonstrated that analytically pure **3a** was obtained quantitatively. Similarly, Ph_3PAuI (**5a**) was isolated by a similar treatment of **1a** with $CH_3C(O)I$ (**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_2Cl_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.



(2)



(3)

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

Genaral 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_3PO_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_6D_6) δ 33.41

3a: ^{31}P NMR (160 MHz, C_6D_6) δ 35.17

5a: ^{31}P NMR (160 MHz, C_6D_6) δ 39.69

1b: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 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}H NMR (400 MHz, CD_2Cl_2) δ 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}H NMR (400 MHz, CD_2Cl_2) δ 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, 2 H), 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}P and ^{1}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_6H_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 $CH_3C(O)Cl$ (**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 $CH_3C(O)I$ (**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_2Cl_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

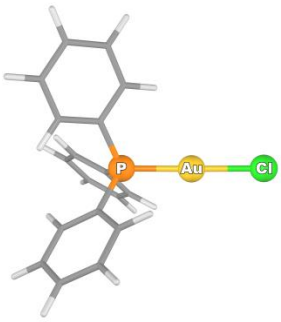
The DFT calculations of the equilibrium structures and the energetics of the intermediates and transition states were carried out by the GAUSSIAN09 suite of programs.[3,4] The following basis set was employed with M06 functional: 6-31G(d,p) for, Cl, Br, and P atoms as well as C and O atoms of the carbonyl 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.

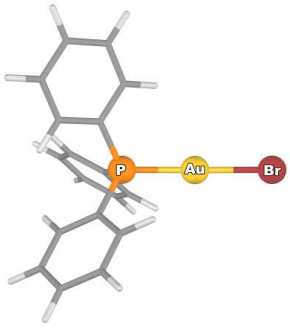
Table S1. The calculated energies of the reactants (**1a** and **2**), **TS7**, intermediate (**8**) the transition states (**TS10** and **TS11**), and products (**3a** and **4**) for the halogen exchange reaction between Au(Cl)(PPh_3) (**1a**) and Me(CO)Br (**2**). (1 a.u. = 2625.50 kJ/mol)

Compounds	E (a.u.)	Imaginary freq. (cm^{-1})	E_a (kJ/mol)
Au(Cl)PPh_3 (**1a**)	-1629.76146040	–	–
Acetyl bromide (**2**)	-2724.70207200	–	–
Au(Br)PPh_3 (**3a**)	-3741.15392858	–	–
Acetyl chloride (**4**)	-613.32523747	–	–
Zero-point energy			
Au(Cl)PPh_3 (**1a**)	-1629.470632	–	–
Acetyl bromide (**2**)	-2724.655231	–	–
Au(Br)PPh_3 (**3a**)	-3740.863395	–	–
Acetyl chloride (**4**)	-613.277769	–	–
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

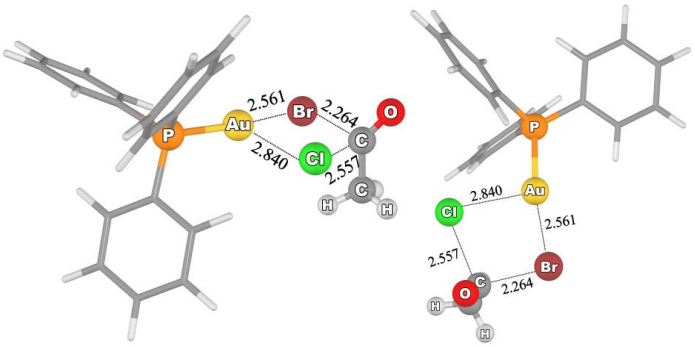
Structures of reactants, intermediates, transition states, and products



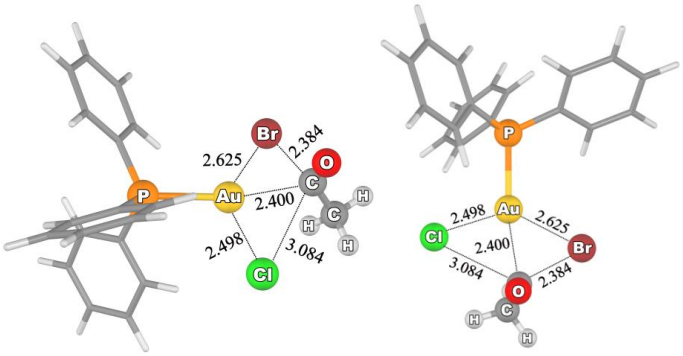
1a



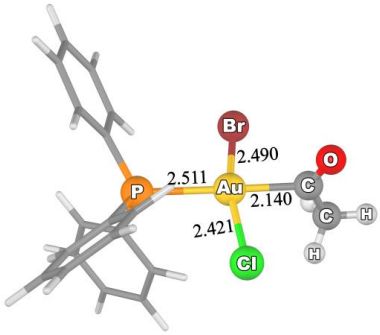
3a



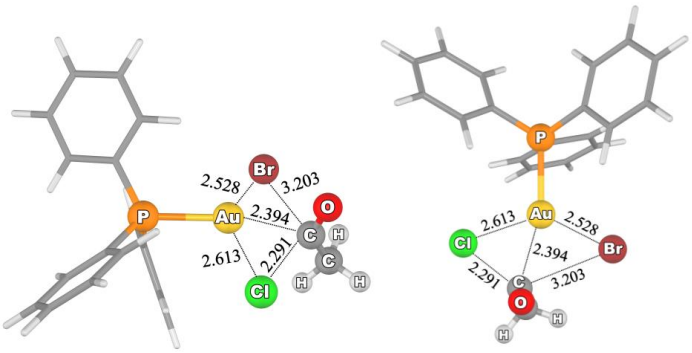
TS7



TS10



8



TS11

3-5 References and Notes

[1] For the conventional Cl-to-Br and Cl-to-I conversion of Au(I) complexes, see: LiBr and LiI: (a) McAuliffe, C. A.; Parish, R. V.; Randall, P. D. *J. Chem. Soc*., *Dalton Trans*. **1979**, 1730. (b) Barnes, N. A.; Flower, K. R.; Fyyaz, S. A.; Godfrey, S. M.; McGown, A. T.; Miles, P. J.; Pritchard, R. G.; Warren, J. E. *CrystEngComm* **2010**, *12*, 784. KBr and KI: (c) Schneider, D.; Schier, A.; Schmidbaur, H. *Darton Trans*. **2004**, 1995. (d) Ramírez, J.; Sanaú, M.; Fernández, E. *Angew. Chem*., *Int. Ed*. **2008**, *47*, 5194. $AgNO_3$/NaBr: (e) El-Etri, M. M.; Scovell, W. M. *Inorg. Chem*. **1990**, *29*, 480. HBr: (f) Johnson, B. F. B.; Lewis, J.; Nicholls, J. N.; Puga, J.; Whitmire, K. H. *J. Chem. Soc.*, *Dalton Trans*. **1983**, 787.

[2] Frisch, M. J. T., G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09, Revision B. 01, Gaussian Inc., Wallingford CT, **2009**.

[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.

[4] For the oxidative addition to Au(I) complexes giving Au(III) complexes, see: (a) Attar, S.; Nelson, J.; Bearden, H. W. H.; Alcock, N. W.; Solujic, L.; Milosavljevic, E. B. *Polyhedron* **1991**, *10*, 1939. (b) Tamaki, A.; Kochi, J. K. *J. Chem. Soc., Dalton Trans.* **1973**, 2620. (c) Johnson, A.; Puddephatt, R. J. *J. Organomet. Chem.* **1975**, *85*, 115. (d) Pearson, R. G.; Figdore, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 1541.

[5] Gregory, B. J.; Ingold, C. K. *J. Chem. Soc. B*, **1969**, 276.

Chapter 3

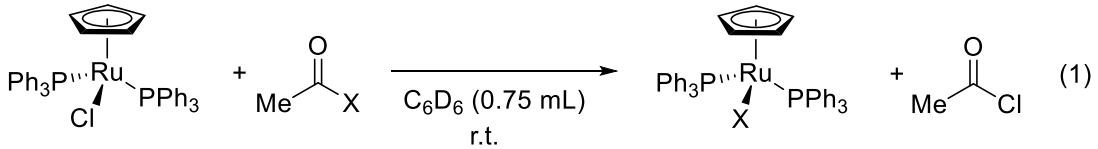
Ligand Exchange Reaction of Ruthenium Complexes with Acid Halides

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 filtra-tion, extraction, drying in the presence of desiccant, and recrystalliza-tion, were omitted. Herein, the Cl-to-X conversion of a ruthenium chloride is described along with its mechanistic study. [1-3]

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_6D_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** (δ 40.1) to CpRu(Br)(PPh_3)$_2$ (**3**) (δ 39.0) and MeC(O)Cl (**4**) was observed (6.3% of **3** after 0.5 h).[4] 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**) (δ 38.0) after 2.5 h at room temperature.

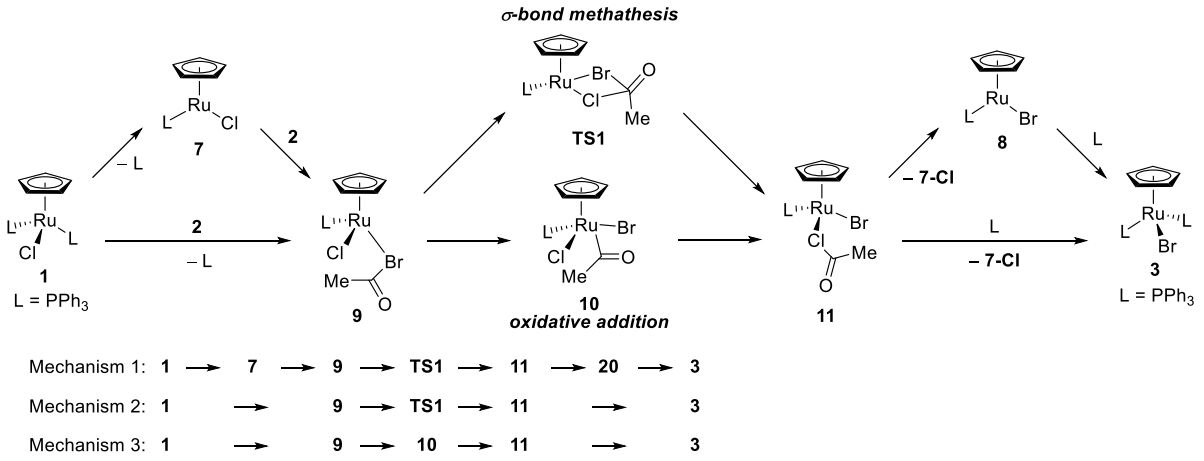


X = Br **2**;	0.5 h	X = Br, **3**; 6.3%	—
X = Br **2**;	9 h	X = Br, **3**; quant.	quant. **4**
X = I **5**;	2.5 h	X = I, **6**; quant.	quant. **4**

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_6H_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 mechnism 1, The liberation of PPh$_3$ produces the coordinately unsaturated CpRu(Cl)(PPh$_3$) (**7**). Next, σ-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]



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 σ-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).

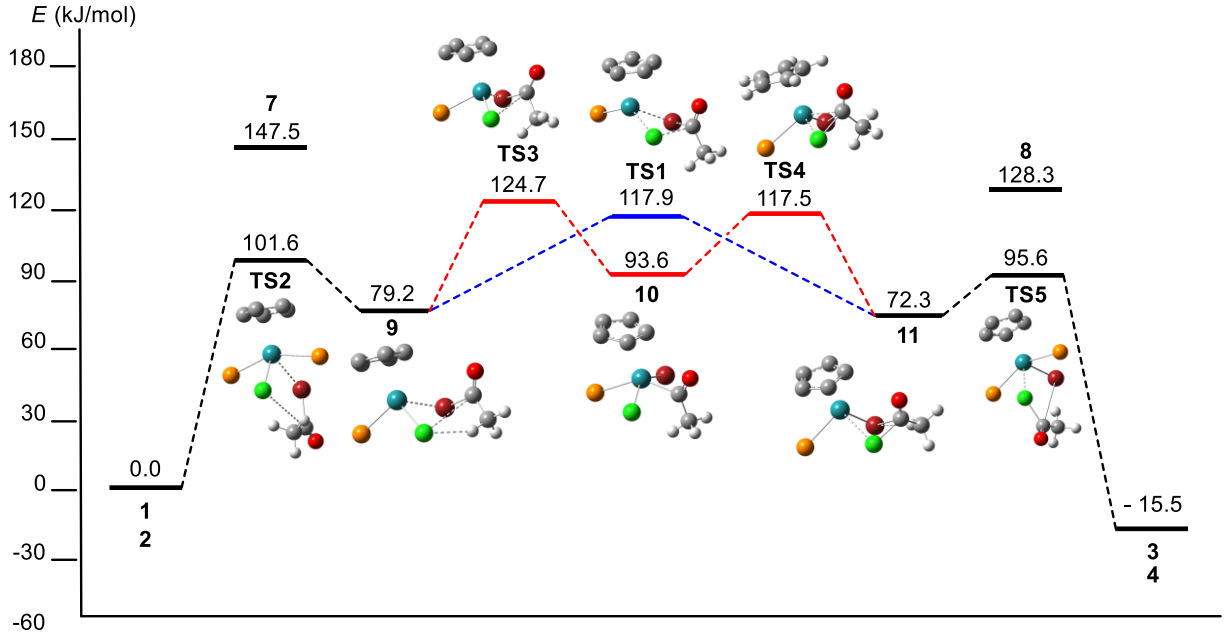
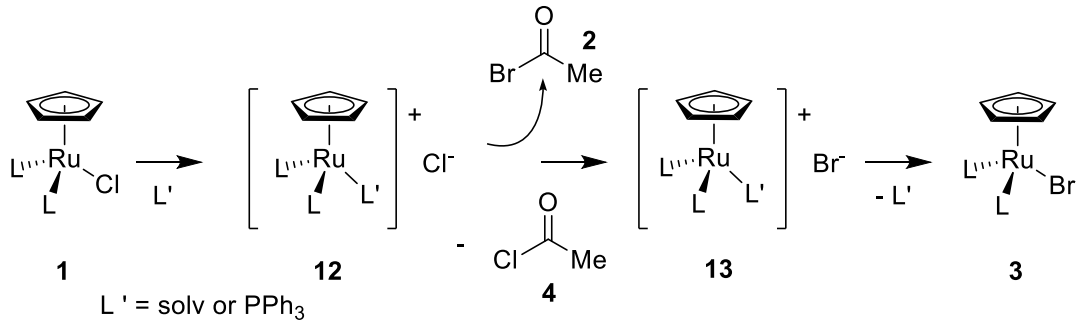


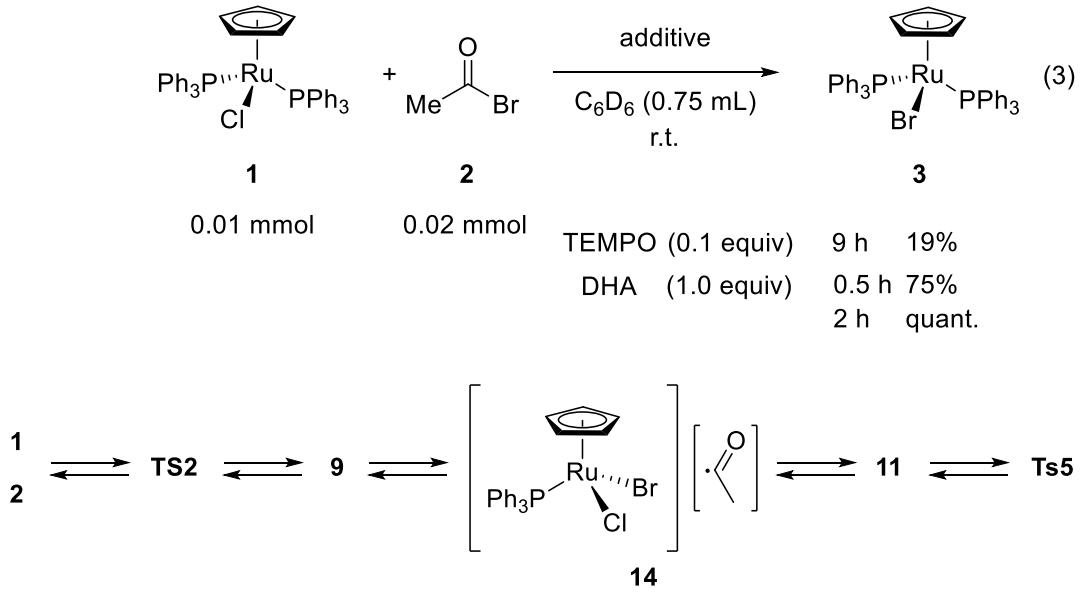
Figure 1. Energy diagram for the reaction of **1** with **2**. Phenyl of PPh_3 and hydrogen atoms of Cp are omitted for clarity. Atoms in blue, orange, green, dark red, and red represent Ru, P, Cl, Br, and O, respectively.

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**.[8] 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.[9] 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.[10] 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 $CH_3C(O)\cdot$ 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 $CpRu(Cl)(PPh_3)_2$ reaction. Moreover, DFT calculations suggest that the associative liberation of PPh_3 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_3PO_4 (aq) as an external standard, and $S{=}P(C_6H_4OMe\text{-}p)_3$ 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. $CpRu(Cl)(PPh_3)_2$ (**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, C_6D_6) δ 40.10, **3:** ^{31}P NMR (160 MHz, C_6D_6) δ 38.97, **6:** ^{31}P NMR (160 MHz, C_6D_6) δ 37.97

A ligand exchange reaction between Cl of CpRu(Cl)(PPh_3)$_2$ (1) and Br of MeC(O)Br (2) (Eq. 2)

Into a dry Pyrex NMR tube were added a solution of CpRu(Cl)(PPh_3)$_2$ (1, 0.010 mmol, 500 μL/20 mM in benzene-d_6), a solution of S=P(C_6H_4OMe-*p*)$_3$ (0.0050 mmol, 50 μL/100 mM in benzene-d_6), and benzene-d_6 (180 μL). After the sensitivity of **1** to the internal standard was measured by ^{31}P NMR spectroscopy, a solution of MeC(O)Br (2, 0.020 mmol, 20 mL/1.0 M in benzene-d_6) was added and the reaction was monitored by ^{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%.

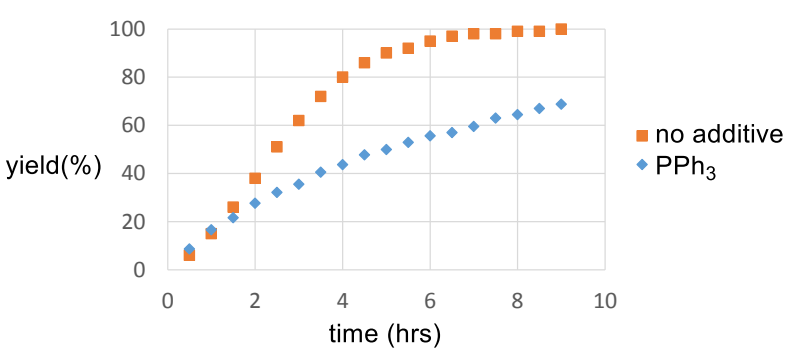
Preparative scale ligand exchange reactions

Into a 100 mL flask were added CpRu(Cl)(PPh_3)$_2$ (**1**, 726.2 mg, 1.0 mmol), MeC(O)Br (**2**, 614.8 mg, 5.0 mmol), and C_6H_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_3)$_2$ (**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_3

Into a dry Pyrex NMR tube were added a solution of CpRu(Cl)(PPh_3)$_2$ (**1**, 0.010 mmol, 500 μL/20 mM in benzene-d_6), a solution of S=P(C_6H_4OMe-*p*)$_3$ (0.0050 mmol, 50 μL/100 mM in benzene-d_6), a solution of PPh_3 (0.0010 mmol, 10 μL/100 mM in benzene-d_6), and benzene-d_6 (170 μL). After the sensitivity of **1** to the internal standard was measured by ^{31}P NMR spectroscopy, a solution of MeC(O)Br (**2**, 0.020 mmol, 20 mL/1 M in benzene-d_6) was added and the reaction was monitored by ^{31}P NMR spectroscopy and the result was compared with that of the reaction carried out without the addition of free PPh_3 (Figure S1), demonstrating that the ligand exchange reaction is retarded by the addition of PPh_3.

Figure S1



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 PPh_3. 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 PPh_3, 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 PPh_3 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).

parameters	**TS2**	**9**	**TS1**	**TS3**	**11**	**10**	**TS5**	**TS4**
∠Ru-Cl-Br-C	179.8	116.0	137.9	102.1	104.0	104.8	179.9	93.6
∠Cl-Ru-Br	99.3	85.2	79.2	123.4	59.5	139.7	102.4	123.0
∠Cl-C-Br	76.1	79.2	92.7	104.5	86.2	108.5	67.8	101.9
Ru-Cl	2.66	2.46	2.67	2.41	3.27	2.48	2.78	2.79
Ru-Br	3.33	3.19	2.76	2.84	2.56	2.55	2.86	2.52
Cl-C	4.62	3.69	2.35	3.54	1.86	2.79	1.90	2.11
Br-C	2.05	2.03	2.43	2.23	4.13	3.03	4.75	3.76
Ru-C	4.54	3.77	3.49	2.49	3.80	2.10	4.23	2.46

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})

compounds	*E* (a.u.)	E_{ZPC}[a] (a.u.)
$CpRu(Cl)(PPh_3)_2$ (**1**) (Cs)	-2815.56602	-2814.90177
MeC(O)Br (**2**)	-2724.31386	-2724.26448
TS2	-5539.83805	-5539.12756
9	-4505.82482	-4505.40059
TS1	-4505.80813	-4505.38583
11	-4505.82888	-4505.40322
TS5	-5539.84505	-5539.12984
MeC(O)Cl (**4**)	-613.23369	-613.18371
$CpRu(Br)(PPh_3)_2$ (**3**) (Cs)	-4926.65266	-4925.98845
PPh_3	-1034.02569	-1033.73551
$CpRu(Cl)(PPh_3)_2$ (**7**)	-1781.48250	-1781.11010
$CpRu(Br)(PPh_3)$ (**8**)	-3892.57022	-3892.19816
TS3	-4505.80740	-4505.38326
10	-4505.81909	-4505.39510
TS4	-4505.81061	-4505.38600
14	-4352.83229	-4352.45495
MeC(O)	-152.99438	-152.94855

[a] with zero-point energy correction

IRC analysis

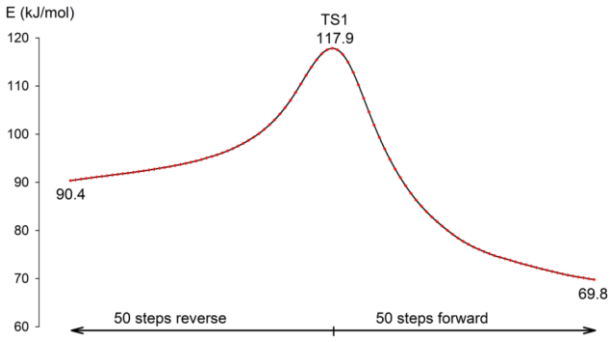


Figure S2. From **9** to **11** via **TS1**.

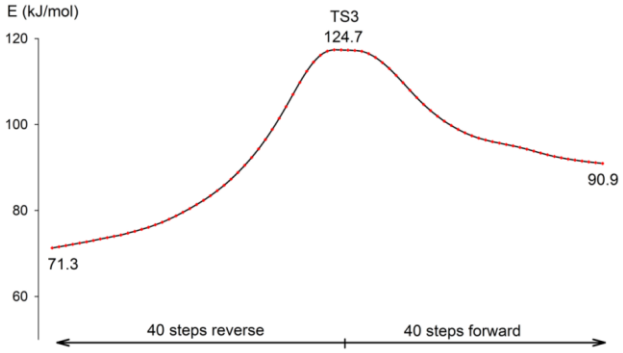


Figure S3. The IRC energy diagram of the transformation from **9** to **10** via **TS3**.

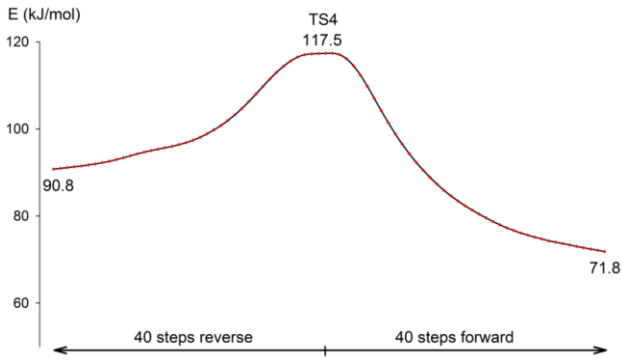
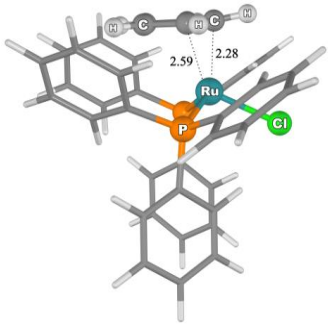
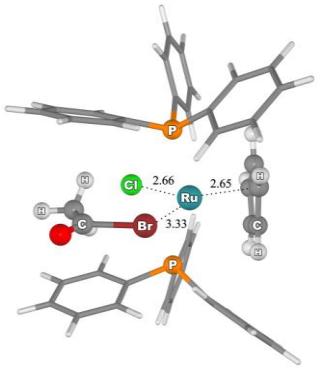


Figure S4. The IRC energy diagram of the transformation from **10** to **11** via **TS4**.

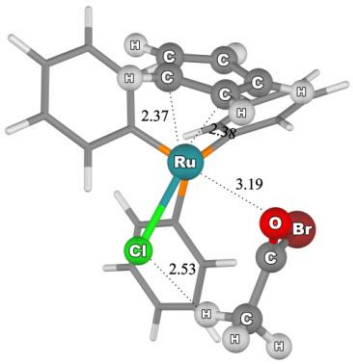
Structures of reactants, intermediates, transition states, and products



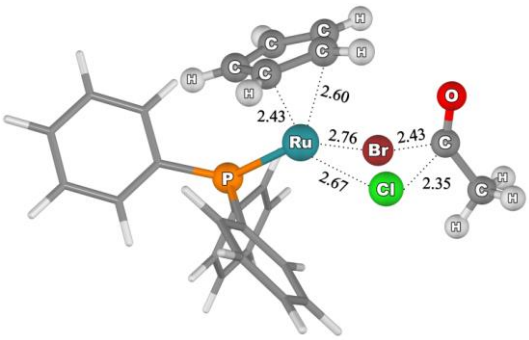
1



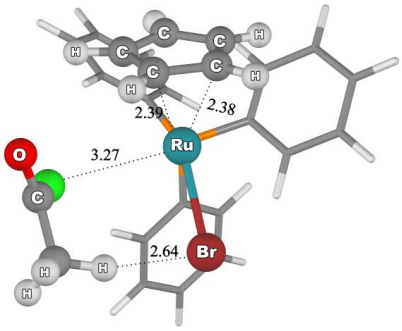
TS2



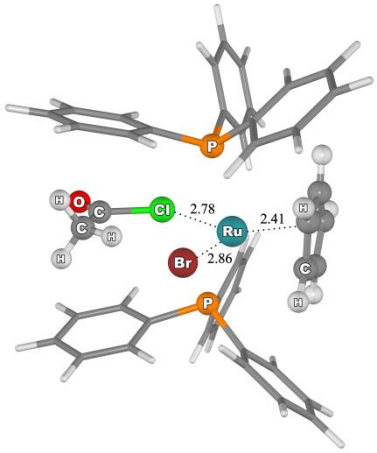
9



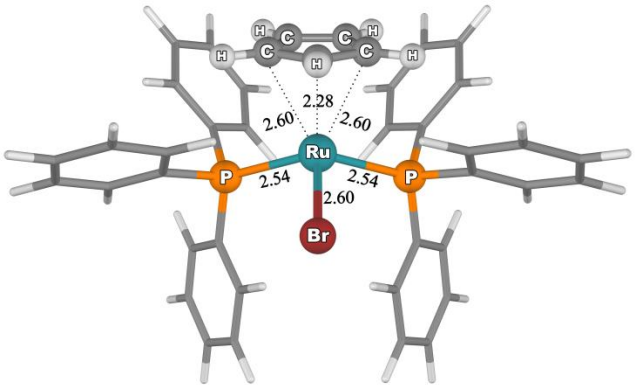
TS1



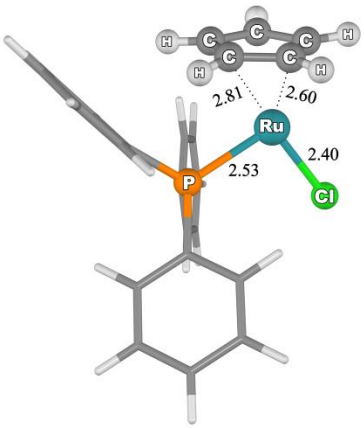
11



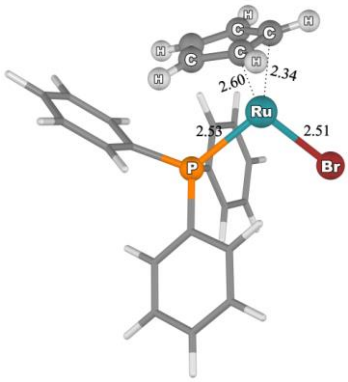
TS5



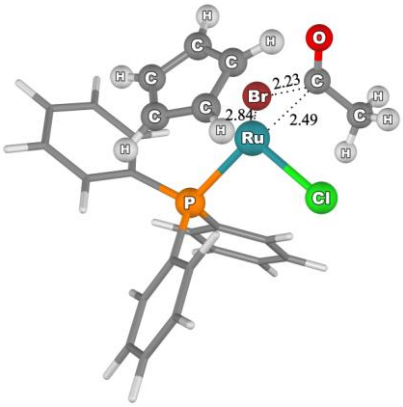
3



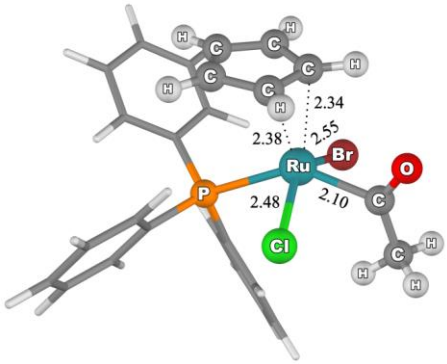
7



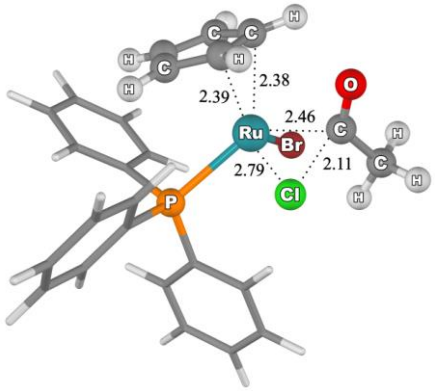
8



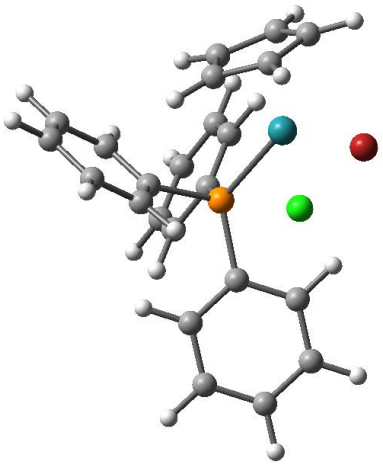
TS3



10



TS4



14

3-5 References and Notes

[1] For Ru-Cl to Ru-Br conversion with MBr, see: (a) de los Ríos, I.; Tenorio, M. J.; Padilla, J.; Puerta, M.C.; Valerga, P. *J. Chem. Soc., Dalton Trans.* **1996**, 377. (b) Brunner, H.; Muschiol, M.; Tsuno, T.; Takahashi, T.; Zabel, M. *Organometallics* **2010**, *29*, 428. (c) Haines, R. J.; du Preez, A. L. *J. Organomet. Chem.* **1975**, *84*, 357.

[2] For Ru-Cl to Ru-I conversion with MI, see: (a) Albers, M. O.; Robinson, D. J.; Shaver, A.; Singleton, E. *Organometallics* **1986**, *5*, 2199. (b) Koelle,U.; Kossakowski, J. *J. Organomet. Chem.* **1989**, *362*, 383. (c) Bosch, H. W.; Hund, H.; Nletlispach, D.; Salzer, A. *Organometallics* **1992**, *11*, 2087.

[3] For the reactions using HX, see: (a) Romerosa, A.; Campos-Malpartida, T.; Lidrissi, C.; Saoud, M.; Serrano-Ruiz, M.; Peruzzini, M.; Garrido-Cárdenas, J. A.; García-Maroto, F. *Inorg. Chem.* **2006**, *45*, 1289. (b) Kaulen, C.; Pala, C.; Hu, C.; Ganter, C. *Organometallics* **2001**, *20*, 1614. (c) Cesarotti, E.; Angoletta, M.; Walker, N. P. C.; Hursthouse, M. B. *J. Organomet. Chem.* **1985**, 286, 343. (d) Fagan, P. J.; Mahoney, W. S.; Calabrese, J. C.; Williams, I.D. *Organometallics* **1990**, *9*, 1843. (e) Conroy-Lewis, F. M. Redhouse, A. D.; Simpson, S. J.; *J. Organomet. Chem.* **1989**, 366, 357.

[4] For the preparations of **3** and **6** from **1**: (a) Yang, Y.; Abboud, K. A.; McElee-White, L. *Dalton Trans.*, **2003**, 4288. (b) Wilczewski, T.; Bocheńska, M.; Biernat, J. F.; *J. Organomet. Chem.* **1981**, *215*, 87-96. (c) Tenaglia, A. *Synlett.* **2003** 2333. (d) Nagashima, H.; Mukai, K.; Shiota, Y.; Yamaguchi, K.; Ara, K.; Fukahori, T.; Suzuki, H.; Akita, M.; Moro-oka, Y.; Itoh, K. *Organometallics* **1990**, *9*, 799-807.

[5] Frisch, M. J. T., G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.;

Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09, Revision B. 01, Gaussian Inc., Wallingford CT, **2009**.

[6] (a) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Account* **2008**, *120*, 215. (b) Zhao, Y.; Truhlar, D. G. *Chem. Phys. Lett*. **2011**, *502*, 1. (c) Zhao, Y.; Truhlar, D. G. *J. Chem. Theor. Comput*. **2011**, *7*, 669. (d) Mantina, M.; Valero, R.; Truhlar, D. G. *J. Chem. Phys*. **2011**, *131*, 064706−1. (e) Kang, R.; Yao, J.; Chen, H. *J. Chem. Theor. Comput*. **2013**, *9*, 1872.

[7] For Ru(IV) complexes formed by the oxidative addition to Ru (II), see: (a) Nagashima, H.; Mukai, K.; Shiota, Y.; Yamaguchi, K.; Ara, K.; Fukahori, T.; Suzuki, H.; Akita, M.; Moro-oka, Y.; Itoh, K. *Organometallics* **1990**, 9, 799-807. (b) Nagashima, H.; Mukai, K.; Itoh, K. *Organometallics*, **1984**, 3, 1314-1315. (c) Nagashima, H.; Mukai, K.; Shiota, Y.; Ara, K.; Itoh, K.; Suzuki, H.; Oshima, N.; Moro-oka, Y. *Organometallics* **1985**, 4, 1314-1315. (d) Perekalin, D. S.; Karslyan, E. E.; Trifonova, E. A.; Konovalov, A. I.; Loskutova, N. L.; Nelyubina, Y. V.; Kudinov, A. R. *Eur. J. Inorg. Chem.* **2013**, 481-493.

[8] For cationic Ru-complexes, see:(a) Treichel, P. M.; Vincenti, P. J. *Inorg. Chem.* **1985**, *24*, 228-230. (b) Haines, R. J.; du Preez, A. L. *J. Organomet. Chem.* **1975**, *84*, 357-367. (c) Ashok, R. F. N.; Gupta, M.; Arulsamy, K. S.; Agarwala, U. C. *Inorg. Chim. Acta* **1985**, *98*, 161-167. (d) Ashok, R. F. N.; Gupta, M.; Arulsamy, K. S.; Agarwala, U. C. *Can. J. Chem.* **1985**, *63*, 963-970. (e) Amarasekera, J.; Rauchfuss, T. B. *Inorg. Chem.* **1989**, *28*, 3875-3883. (f) Brunner, H.; Muschiol, M.; Tsuno, T.; Takahashi, T.; Zabel, M. *Organometallics* **2010**, *29*, 428-435. (g) Bryndza, H. E.; Domaille, P. J.; Paciello, R. A.; Bercaw, J. E. *Organometallics* **1989**, *8*, 379-385.

[9] (a) Howell, B. A.; Debney, M. F.; Rajaram, C. V. *Thermochimica Acta* **1992**, *212*, 115-122. (b) Akaba, R.; Iwasaki, M.; Matsumura, T.; Kamata, M.; Itoh, H. *J. Phys. Org. Chem.* **1996**, 9, 187-190.

[10](a) Fernandez-Zumel, M.; Thommes, K.; Kiefer, G.; Sienkiewicz, A.; Pierzchala, K.; Severin, K.; *Chem. Eur. J.* **2009**, 15, 11601-11607. (b) Bland, W. J.; Davis, R.; Durrant, J. L.

A. *J. Organomet. Chem.* **1985**, *280*, 357-406. (c) Thommes, K.; Içli, B.; Scopelliti, R.; Severin, K. *Chem. Eur. J.* **2007**, *13*, 6899–6907. (d) Quebatte, L.; Thommes, K.; Severin, K. *J. Am. Chem. Soc.* **2006**, *128*, 7440-7441.

[11] Wilczewski, T. *J. Organomet. Chem.* **1986**, *317*, 307-325.

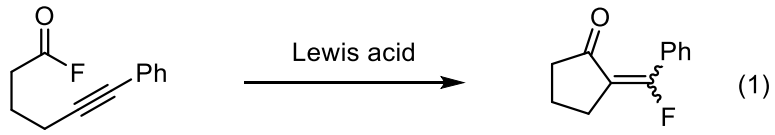
Chapter 4

Lewis Acid Catalyzed Intramolecular Acylfluorination of Alkynes

4-1 Introduction

Organicfluorine 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.[1] Fluoroalkene moiety is regarded as peptide mimics, therefore it has potential applications in medicinal chemistry.[2]

It is known that the addition reaction of the acid chloride to alkynes takes place by using transition-metal catalysts[3] or Lewis acids[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).



(1)

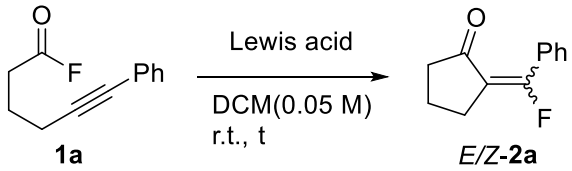
4-2 Results and Discussion

Initially we treated the acid fluoride **1a** bearing alkyne moiety using 10 mol% of $BF_3{\cdot}OEt_2$ as a Lewis acid with strring 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 $B(OEt)_3$ and BPh_3 were used as a Lewis acid catalyst, the product **2a** were gained in only trace amount (entries 4 and 5). The use of $B(C_6H_5)_3$ was less efficient in the acylfluorination of **1a** than the use of $BF_3{\cdot}OEt_3$ (entry 6). Non-boron-based Lewis acid such as $AlCl_3$, $FeCl_3$, $ZnCl_2$ 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 $BF_3{\cdot}OEt_2$ in CD_2Cl_2 at room temparature by ^{19}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 $BF_3{\cdot}OEt_2$ 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**.

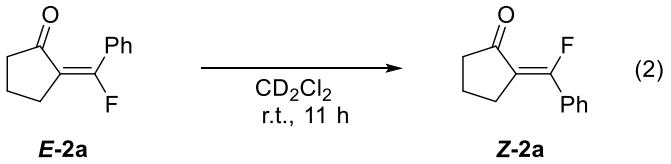
Table 1. Optimization of the Reaction Conditions



1a *E/Z*-**2a**

Entry	Lewis Acid	Catalyst Lording [mol%]	*t* [h]	Yield [%][a]	*E*/*Z*[a]
1	BF_3•OEt_2	5	12	94	3/1
2	BF_3•OEt_2	5	2	67	8.6/1
3	BF_3•OEt_2	10	2	91	5.5/1
4	$B(OEt)_3$	10	12	trace	-
5	BPh_3	10	12	trace	-
6	$B(C_6F_5)_3$	10	12	52	2/1
7	$AlCl_3$	10	12	8	1/1
8	$FeCl_3$	10	12	28	2.1/1
9	$ZnCl_2$	10	12	trace	-

DCM = dichrolomethane [a] Yields and ratios of *E*/*Z* were determined by ^{19}F NMR using PhF as an internal standard.



***E*-2a** ***Z*-2a** (2)

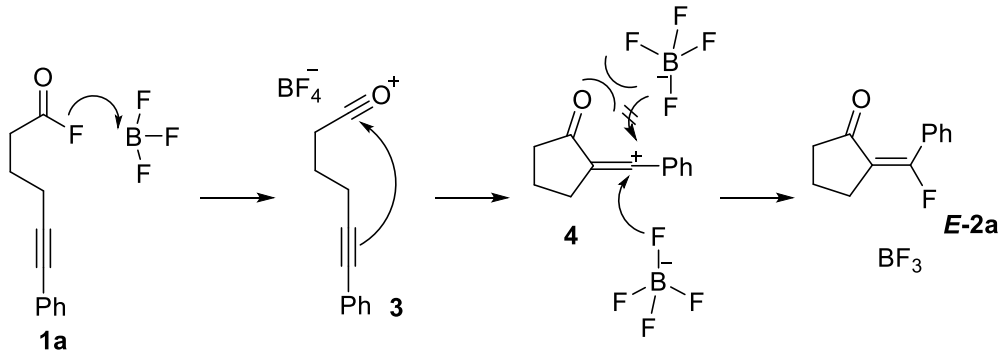
with $BF_3{\cdot}OEt_2$(10 mol%) *E*/*Z* = 2.2/1

without $BF_3{\cdot}OEt_2$ *E*/*Z* = >99/1

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^-.[5] 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_4^- anion approaches to the opposite side of the carbonyl group due to its electronic and steric hindrance.

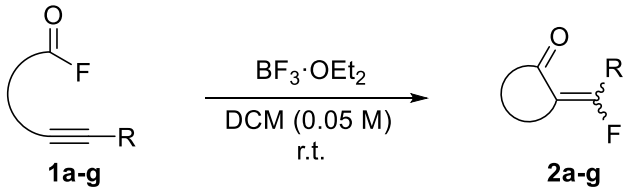
The results of the intramolecular acylfluorinations of various substrates **1a-g** are summarized in Table 2. The reaction of substrate **1b** bearing electron-poor aryl group (*p*-CF_3-C_6H_4) in the presence of 10 mol% of $BF_3{\cdot}OEt_2$ for 12 hours afforded the desired product **2b** in 68% isolated 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 $BF_3{\cdot}OEt_2$ for 24 hours produced **2d** in 87% yield with high selectivity (*E*/*Z* = 18/1). Similarly, use of the substrate (**1e**)

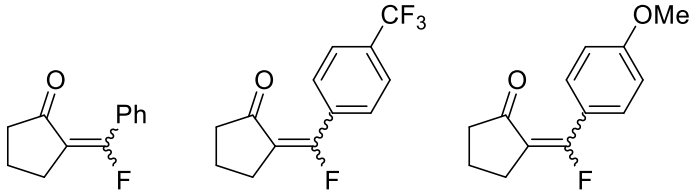
containing NTs tether in the arm resulted in high selectivity (*E/Z* = >99/1). In the cases of substrates with shorter or longer alkyl chain than **1a**, the acylfluorination products (**2f** or **2g**) were not yielded.



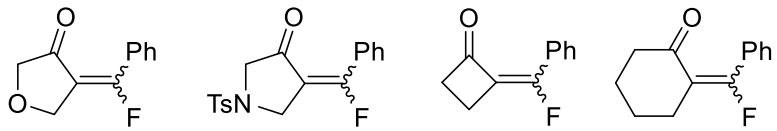
Scheme 1. Proposed Mechanism for the Intramolecular Acylfluorination

Table 2. Scope and Limitations[a]





2a	**2b**	**2c**
85%[b]	68%[b]	Trace
E/Z = 5.5/1	*E/Z* = 4.3/1	(2 h)
(2 h)	(12 h)	



2d	**2e**[c]	**2f**	**2g**
87%[b]	68%[b]	N.D.	N.D.
E/Z = 18/1	*E/Z* = >99/1		
(24 h)	(2 h)		

[a] **1** (0.5 mmol), $BF_3{\cdot}OEt_2$ (10 mol%), and DCM (10 mL) at r.t.

[b] Isolated yield [c] 40 mol% of $BF_3{\cdot}OEt_2$

4-3 Conclusions

We demonstrated the intramolecular fluoroacylation of alkynes was achieved by employing $BF_3 \cdot OEt_2$ 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

Genaral Comments

The ^1H, ^{13}C and ^{19}F NMR spectra in $CDCl_3$ and CD_2Cl_2 were measured with a ECS400 (400 MHz) spectrometer. The chemical shifts in the ^1H NMR spectra were recorded relative to Me_4Si as an internal standard, and the chemical shifts in the ^{13}C NMR spectra were recorded relative to $CHCl_3$ (δ 77.0). CD_2Cl_2 was purified by distillation from P_2O_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), $BF_3 \cdot OEt_2$ (0.05 mmol) , and the reaction mixture was stirred for 2 hrs at roomtemparature and then was quenched by sat. $NaHCO_3$. The resulting mixture was poured sat. NaCl and extracted with Et_2O. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressre 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 purerified by silicagel column chromatography.

***E*-2a**: 72% yield; pale yellow oil; ^1H 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; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 2 H), 7.47 (m, 3 H), 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)

Tipical Procedure for Synthesis of Acid Fluoride 1a

To a solution of 6-phenyl-5-hexynoic acd(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%). ^1H 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, $CDCl_3$): δ 45.95.

4-5 References and Notes

[1] (a) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308-319. (b) Begue, J.-P.; Bonnet-Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*; John Wiley & Sons: Hoboken, NJ, 2008. (c) Kirsch, P. *Modern Fluoorganic Chemistry*; Wiley-VCH: Weinheim, Germany, 2004. (d) Mikami, K.; Itoh, Y.; Yamanaka, M. *Chem. Rev.* **2004**, *104*, 1-16.

[2] For reviews, see; (a) Landelle, G.; Bergeron, M.; Turcotte-Savard, M.; ois Paquin *J. Chem. Soc. Rev.* **2011**, *40*, 2867–2908. (b) Yanai, H.; Taguchi, T. *Eur. J. Org. Chem.* **2011**, 5939–5954.

[3] (a) Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6668. (c) Kashiwabara, T.; Kataoka, K.; Hua, R.; Shimada, S.; Tanaka, M. *Org. Lett.* **2005**, *7*, 2241. (d) Sugihara, T.; Satoh, T.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4672.

[4] (a) Price, C. C.; Pappalardo, J. A. *J. Am. Chem. Soc.* **1950**, *72*, 2613. (b)Benson, W. R.; Pohland, A. E. *J. Org. Chem.* **1964**, *29*, 385. (c) Martens. H.; Hoornaert. G. *Tetrahedron Lett.* **1970**, *21*, 1821. (d) Martens, H.; Janssens, F.; Hoornaert, G. *Tetrahedron* **1975**, *31*, 177. (e)Zhou, H.; Zeng, C; Ren, L.; Liao W.; Huang, X. *Synlett* **2006**, 3504. (f) Wang, B.; Wang, S.; Li, P.; Wang, L. *Chem. Commun*. **2010**, *46*, 5891. (g)Hosseini-Sarvari, M.; Mardaneh, Z. *Bull. Chem. Soc. Jpn.* **2011**, 84, 778.

[5] Olah, G. A.; Kuhn, S. J.; Tolgyesi, W. S.; Baker, E. B. *J. Am. Chem. Soc*. **1962**, *84*, 2733-2740.

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 discribed. The reaction between *trans*-M(X)[C(O)Ph](PPh_3)$_2$ and PhC(O)X' (M = Pt, Pd; X, X' = Cl, Br, I) successfully gave a clean equilibrium mixture. The Gibbs free energy (ΔGs) was equivalent to the $\Delta\Delta G$ of the oxidative additions of PhC(O)X and PhC(O)X' to M(PPh_3)$_2$L$_n$ (L$_n$ = 2PPh_3 or CH_2=CH_2). Both experimental and computational studies supported the concerted σ-bond metathesis mechanism. The reaction are used as a very convienient 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 discribed. The complexes of the formula Au(X)(L) (X = Br and I; L = PPh_3 and IPr) were conveniently prepared by a quite simple procedure using the treatment of Au(Cl)(L) with CH_3C(O)X. The mechanistic study by DFT calculation supported that the reaction proceeded through the concerted σ-bond metathesis

In chapter 3, the halogen exchange reactions between ruthenium complexes and acid halides are discribed. The treatment of CpRu(Cl)(PPh_3)$_2$ with MeC(O)X provides a very convenient procedure for the synthesis of CpRu(X)(PPh_3)$_2$. The proposed mechanism involves an intermediate produced by the concerted liberation of PPh_3 by the incoming 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 (BF_3·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 Δ*G* 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
   Organometallics **2013**, 32, 2026-2032.

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
   Chem. Lett. **2013**, *42*, 831-832.

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
   J. Organomet. Chem. **2014**, *769*, 34-37.

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

Acknowledgement

The author would like to express his appreciation and gratitude to Professor Nobuaki Kambe at the Department of Applied Chemistry, Graduate School of Engineering, Osaka University for a great number of suggestions, discussions and guidance. The author wishes to express his sincere thanks to Professor Naoto Chatani and Professor Makoto Yasuda for kind discussions and close attention to detail with respect to this thesis. The author would like to express his marvelous gratitude to Associate Professor Hitoshi Kuniyasu for valuable suggestions, hearty encouragement and fruitful discussions. The author would like to express his special thanks to Assistant Professor Takanori Iwasaki for passionate discussions and everlasting encouragement.

The author would like to express his marvelous gratitude Professor Masahiro Ehara, Dr. Karan Bobuatong and Dr. Yunpeng Lu, Institute of Molecular Science for their collaboration on theoretical calculation. The author would like to express his special thanks to Professor Shin-ichi Fujiwara and Assistant Professor Susumu Tsuda, the Department of Chemistry, Osaka-Dental University for kind discussion. Thanks are due to the Instrumental Analysis Center, Graduate School of Engineering, Osaka University, for measurement of spectral and analytical data.

The author gratefully wish to thank Grants for Excellent Graduate Schools and Shoshisha Foundation for financial support during his PhD program.

The author would sincerely like to thank Professor Douglas W. Stephan, Department of Chemistry, University of Toronto for giving him opportunity of his overseas education. The author thanks Dr. Manuel Pérez as my supervisor during his overseas education.

The author would like to express his appreciation to Dr. Yasunori Minami, Mr. Kazunobu Takekawa and Mr. Daisuke Nakane for their advice and stimulating discussions. Special thanks are given to Mr. Yuya Komatsu, Mr. Takashi Wakasa, Mr. Masato Nakazaki, Mr Takuya Nakajima and Mr. Daigo Shiozaki for their collaborations and helpful discussions. The author is deeply indebted to Mr. Takehiro Omori, Mr. Ryohei Shimizu, Dr. Daisuke Shiro and Mr. Junjie Li as colleagues for master's and doctor's courses. The author also thanks all other members of the laboratory of Professor Kambe and Ms. Yuko Fujiie as a lab's administrative assistant for helpful discussion, their comfortable assistance and enjoyable days to him.

Finally, the author would like to express thanks to his parents for their understanding and perpetual support.

January, 2015

Atsushi Sanagawa