A Study on the Cyclocarbonylation Catalyzed by Palladium Complexes

パラジウム錯体触媒を用いた環化カルボニル化反応に関する研究

Masakazu Iwasaki

①

A Study on the Cyclocarbonylation Catalyzed by Palladium Complexes

パラジウム錯体触媒を用いた環化カルボニル化反応に関する研究

by

Masakazu Iwasaki

Department of Synthetic Chemistry

Faculty of Engineering

The University of Tokyo

1991

Preface

This is the thesis for a doctorate of the University of Tokyo and the results of 4 years long research work.

Transition metal-catalyzed reaction is one of the most intensively studied fields among organic chemistry. The author studied on the palladium-catalyzed cyclo-carbonylation of cinnamyl compounds mainly by checking the reactivity of various substrates. The results showed its wide applicability for organic synthesis and were so informative for the elucidation of the reaction mechanism.

In Chapter 1, general back ground for the carbonylation reactions and the starting point of author's study on the cyclocarbonylation are described.

In Chapters 2 and 3, the application of the cyclocarbonylation for the synthesis of tricyclic compounds (phenanthrenes) and fused heteroaromatics are described. The results obtained here was so informative for the discussion on the reaction mechanism.

In Chapter 4, the reactivity of the palladium-catalyzed cyclocarbonylation was compared with that of benzannulation reaction of chromium aryl-carbene complexes with alkynes. In some cases, both reactions show similar selectivity on their orientation.

In Chapter 5, another application of the cyclocarbonylation was examined by employing 2,4-pentadienyl compounds as starting materials instead of cinnamyl compounds. The results exemplified a good applicability of the reaction for the synthesis of non-fused phenol derivatives.

In Chapter 6, a novel ketene formation by the reaction of acid chlorides with low-valent platinum complexes is described. This reaction served as a model for the mechanism of the cyclocarbonylation because a possible mechanism of it involved an alkenylketene intermediate.

Acknowledgment

The author wishes to express his most gratitude to the following peoples.

Professor Masanobu Hidai. The supervisor of the author.

Dr. Hiroyuki Matsuzaka, who has instructed and advised the author since the author first joined professor Hidai's group in April, 1985.

Dr. Youichi Ishii, who instructed the author especially on the theory and techniques of organic synthesis.

Dr. Yukio Koyasu, who first developed the palladium catalyzed cyclocarbonylation and has often given good advises even after his graduation.

Mr. Yoshihiro Kobayashi, who carried out a large part of the experiments in chapter 3 and almost all experiments in chapter 6.

Mr. Ji-Ping Li from Liao-Ning Normal University, China, who kindly helped author's work especially on the study described in chapter 3.

Mr. Chao Gao, from China, who carried out most of the experiments in chapter 5.

Mr. Yoshitaka Hiroe, who worked and obtained so many results on the cyclo-carbonylation before the author started his work.

The author also wishes to express his acknowledgment to the following members of Prof. Hidai's, Prof. Uchida's and Prof. Yoshikawa's group.

Dr. Yasushi Mizobe	Dr. Atsushi Fukuoka	Mr. Masanobu Sato
Mr. Kenzo Chikanari	Dr. Tomoaki Tanase	Dr. Katsuaki Ishida
Mr. Takashi Murata	Dr. Tamotsu Takahashi	Dr. Keiko Orisaku
Mr. Takahiko Kojima	Mr. Sho-ichiro Wakabayashi	Mr. Toyohisa Ishida
Mr. Kouichi Sonobe	Mr. Toshitaka Suzuki	Mr. Takayuki Aoshima
Mr. Hiroyuki Oshita	Mr. Kouichi Yoshida	Mr. Seiya Sugiura
Mr. Kiyomi Imagawa	Mr. Masa-aki Kurano	

Table of Contents

List of Publications

Chapter 2.

1) Highly Selective Synthesis of Phenanthryl Acetates by Palladium Catalyzed Cyclocarbonylation of Naphthylallyl Acetates
M. Iwasaki, H. Matsuzaka, Y. Hiroe, Y. Ishii, Y. Koyasu, and M. Hidai
Chem. Lett., 1159–1162 (1988).

Chapter 3.

2) Synthesis of Benzofurans and Benzothiophenes by Palladium Catalyzed Cyclocarbonylation of 3–Furylallyl and 3–Thienylallyl Acetates
M. Iwasaki, J.–P. Li, Y. Kobayashi, H. Matsuzaka, Y. Ishii, and M. Hidai
Tetrahedron Lett., **30**, 95–98 (1989).

3) Palladium–Catalyzed Cyclocarbonylation of 3–(Heteroaryl)allyl Acetates
M. Iwasaki, Y. Kobayashi, J.–P. Li, H. Matsuzaka, Y. Ishii, and M. Hidai
J. Org. Chem., in press.

Chapter 4

4) Palladium–Catalyzed Cyclocarbonylation of 3,3–Di(aryl)allyl Acetates
M. Iwasaki, Y. Ishii, H. Matsuzaka, and M. Hidai
J. Organomet. Chem., in preparation.

Chapter 5

5) Novel Synthesis of Phenol Derivatives by Palladium–Catalyzed Cyclocarbonylation of 2,4–Pentadienyl Acetates
Y. Ishii, C. Gao, M. Iwasaki, and M. Hidai
J. Chem. Soc., Chem. Commun., submitted for publication.

Chapter 6

6) Novel Ketene Formation by Reaction of Acid Chlorides with Low-Valent Platinum Complexes
Y. Ishii, Y. Kobayashi, M. Iwasaki, and M. Hidai
J. Organomet. Chem., in press.

In addition, the author contributed to the following articles.

7) Preparation and Reactivities of trans-[(E-PhCH=CHCH$_2$CO)MBr(PPh$_3$)$_2$] (M = Pd, Pt) as Key Intermediate for Cyclocarbonylation of Cinnamyl Compounds
H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai
Chem. Lett., 377-380 (1988)

8) A Novel Palladium- or Platinum-Catalyzed Cyclocarbonylation Reaction of Cinnamyl Compounds for Synthesis of 1-Naphthol Derivatives
H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai
J. Org. Chem., **53**, 3832-3838 (1988)

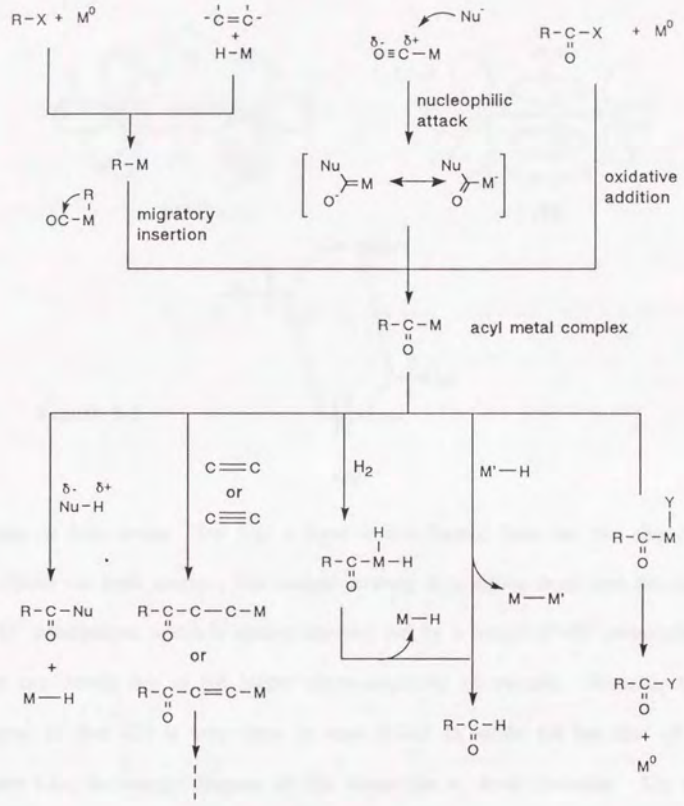
Chapter 1

General Introduction

1-1. General Mechanism for Carbonylation Reactions.

Organic syntheses using metal complexes have attracted much attention for long years because of their good selectivity, mild conditions, or unique reactions hardly attainable by classic methods. Among such reactions, a transition metal-catalyzed carbonylation has long been developed because it can use CO as a carbon source readily obtained from coal or heavy oil by their gasification. The most famous of them are the synthesis of aldehydes from olefins, CO, and H_2 catalyzed by either Co or Rh complexes, the synthesis of acetic acid from methanol and CO in the presence of Rh complexes, and the Fischer-Tropsch hydrocarbon synthesis from CO and H_2. Although the last one is carried out by using heterogeneous catalysts (mainly Fe and Co) in an industrial scale, the reaction itself is closely related to the homogeneous system of carbonylation. As oil became a more useful carbon source in a bulk scale in the recent decades, CO chemistry seemed to lose its industrial role. But the significance of CO chemistry has become evident again by the oil crisis and the growing needs for many kinds of intricate compounds such as drugs or functionalized materials. Under these circumstances, a study on carbonylation reaction is increasing its importance not only for the scientific interest but also for its application in organic synthesis.

Carbonylation reactions invariably involve an acyl-metal intermediates. Considering the importance of this intermediate, the author summarized general pattern of carbonylation in **Scheme 1.1**. The carbonylation consists of mainly two parts; (1) the formation of an acyl-metal intermediate, and (2) the reaction of the acyl-metal intermediate to form another organic moiety. When the second step affords a suitable precursor for the first step, the reaction becomes catalytic. Each part is briefly described in the following sections.



Scheme 1.1 Formation and Reactions of Acyl Complex.

1–2. Formation of Acyl–Metal Intermediate.

Before describing the titled reaction here, the character of CO and its coordination on metal should be summarized.[1)]

The electronic structure of free CO is shown in **Figure 1.1a** (Atomic Orbitals) and **1.1b** (Molecular Orbitals). A σ–bond is formed from the two singly occupied sp

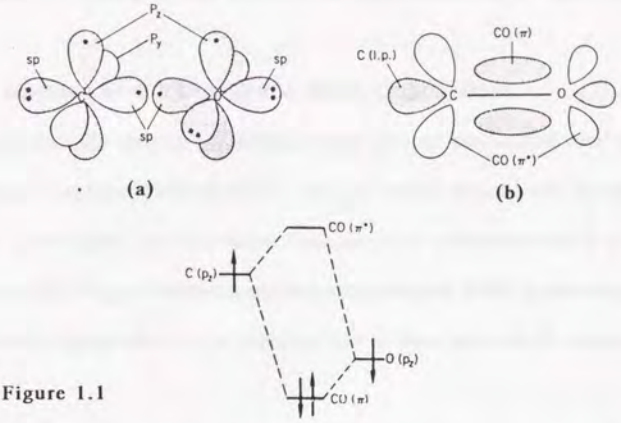


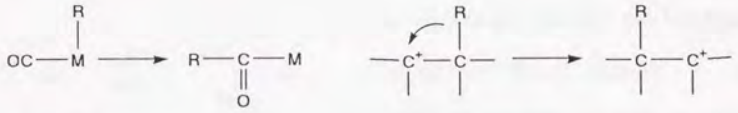
Figure 1.1

orbitals on both atoms. The first π–bond is also formed from the two singly occupied p_z orbitals on both atoms. The second π–bond is a dative bond and this leads to a C^-–O^+ polarization, which is almost canceled out by a partial C^+–O^- polarization of the other two bonds due to the higher electronegativity of oxygen. Actually, the dipole moment of free CO is very close to zero (0.112 D, while CS has that of 1.97 D). **Figure 1.1c**, the energy diagram of CO, shows the π_z–bond character. The π_z–orbital has more character of $O(p_z)$ than $C(p_z)$, while the π*–orbital (LUMO) has more close to $C(p_z)$ than $O(p_z)$. With regard to mononuclear complexes, metals always bind to C, not O, because the HOMO is the lone pair of C and the LUMO is the π* which polarized to C, so the best overlap will be possible at C not O. The sigma donation to metal removes electron density from C and π–back donation increases the electron density of both C and O because the LUMO has both C and O character. As the result, C becomes more positive and O becomes negative upon coordination, that is , CO is made more sensitive for both nucleophilic (on C) and electrophilic attack (on O).

In this way, CO becomes more available for organic reactions by metal complexes.

1-2-1. Insertion of CO Ligand into Metal-Carbon Bond.

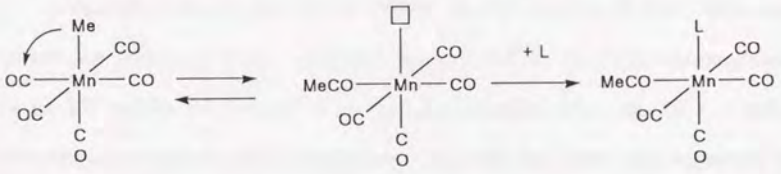
The insertion reaction of carbonyl ligand into an alkyl-metal bond is found for many metal complexes (**Scheme 1.2a**). As the carbon atom of CO ligand is electron deficient (*vide supra*) and has some character of a carbonium ion, it is sometimes compared to the Wagner-Meerwein rearrangement (**Scheme 1.2b**), a non-metallic reaction where an alkyl group moves to a carbonium ion to form rather stable another carbonium ion.



(a) Insertion of CO. **(b)** Wagner-Meerwein Rearrangement

Scheme 1.2

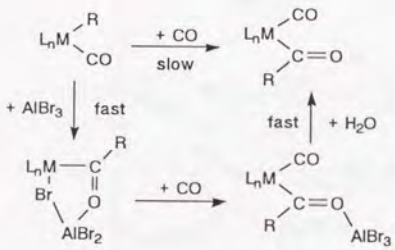
One of the best studied systems for the CO insertion reactions is that of alkyl-manganese-carbonyl complexes by Calderazzo[2] (**Scheme 1.3**). Only *cis*-methyl migration explains the results of $MeMn(CO)_5$ system, i.e., what moves is methyl group and not CO ligand during this "formal" insertion. Therefore, this reaction is often



Scheme 1.3

referred as "migratory insertion".

In this system, a mechanism shown in **Scheme 1.3** is generally accepted, where the CO insertion is reversible and the coordinatively unsaturated acyl complex is trapped by incoming ligand L. Based on the relative rate of insertion for different alkyl groups, it is also found that electron-releasing groups enhance the reaction rate, whereas electron-withdrawing groups slow it down. This effect is possibly due to the relative weakness of the metal-alkyl bonds which changes the activation energy for a transition state between alkyl and acyl complexes.

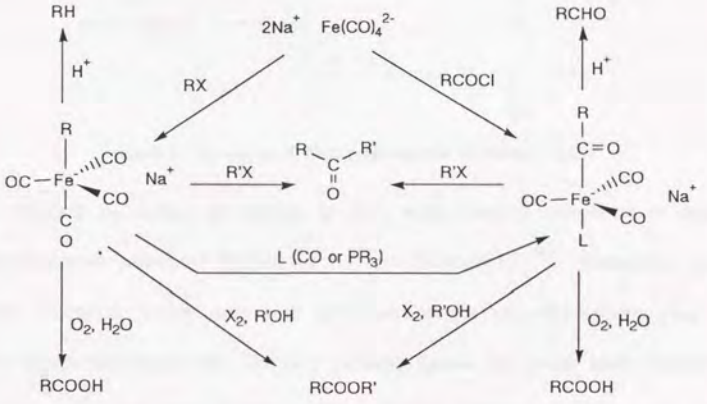


Scheme 1.4

In this manganese system, Shriver and co-workers reported[3] that CO ligand is activated toward insertion by the addition of a Lewis acid such as $AlBr_3$. They explained the results by three functions of Lewis acid (**Scheme 1.4**). 1) Increase of the rate of an alkyl migration, 2) Stabilization of an acyl group, and 3) Providing an electron rich atom which acts as a ligand to fill the vacant site left by the creation of the acyl group.

Although it is not quite certain whether the CO insertion of other alkyl-metal systems are "migratory" or not, Yamamoto also proposed[4] an alkyl migration mechanism for the CO insertion of *cis*- and *trans*-$R_2Pd(L)_2$ complexes (R = Me, Et; L = tertiary phosphine) based on the product distribution. Koga and Morokuma also suggested[5] the alkyl migration mechanism for the system based on the *ab initio* MO calculation of M-$(CH_3)(H)(CO)(PH_3)$ (M = Pd, Pt).

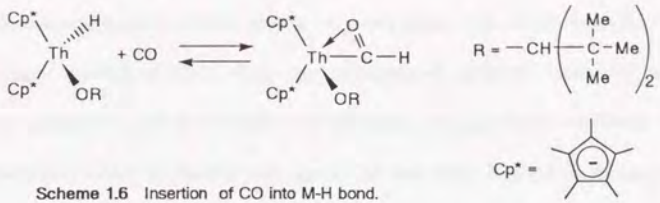
Among synthetic methods using a stoichiometric amount of an acyl complex, the reaction of $Fe(CO)_4^{2-}$, Collman's reagent,[6] would be representative. It reacts with alkyl halides to give the corresponding alkyl-iron complexes. By adding an external ligand such as PPh_3, the CO insertion readily occurs to give acyl complexes which afford various carbonyl compounds by subsequent treatments (**Scheme 1.5**). In this case, the acceleration of the CO insertion by PPh_3 is explained by the stabilization of the coordinatively unsaturated acyl complexes.



Scheme 1.5 Reactions of Collman's reagent.

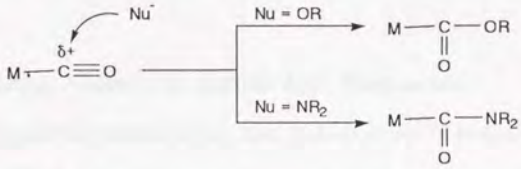
Although the insertion of CO into metal-carbon bonds are often detectable for many transition metal complexes, the CO insertion into metal-hydrogen bonds to form formyl complexes are normally unfavorable possibly due to thermodynamic reasons. But this is not the case when the formyl complexes are stabilized by some other factors. For example, treatment of the thorium-hydride complex, shown in **Scheme 1.6**, with CO affords a formyl complex stabilized by the oxophilicity of thorium to make formyl ligand

coordinate in η^2 mode.[7)]



Scheme 1.6 Insertion of CO into M-H bond.

1-2-2. Nucleophilic Attack on Carbonyl Ligand.



Scheme 1.7 Formation of Alkoxycarbonyl and Carbamoyl Ligand.

Alcohols or amines are known to react with carbonyl complexes to generate alkoxycarbonyl or carbamoyl ligands, respectively (Scheme **1.7**).[8a)] Especially, cationic carbonyl complexes readily react with these nucleophiles not only because they have positive charge themselves but also their carbonyl ligands are poorly back-donated and the carbon atoms are more positive. When neutral carbonyl complexes are starting materials, lithium alkoxides or amides are often used instead of alcohols or amines. In several cases, these reactions lead to the formation of Fischer-carbene complexes,[8b)] although the carbene complex stabilized by an oxygen atom can also be regarded as an anionic acyl complex (**Scheme 1.8**).

It is well-known that the carbon atom of a Fischer-carbene complex is readily react with nucleophiles, which is also characteristic for the

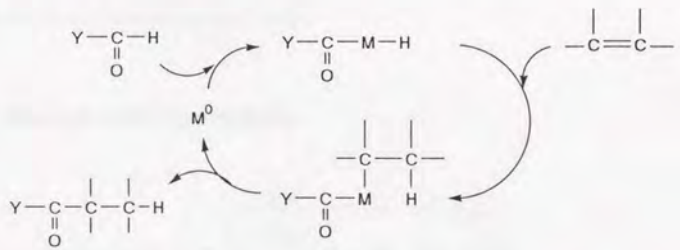
Scheme 1.8 Fischer-Carbene Complex.

carbon atom of acyl complexes (*vide infra*).

Sometimes these reactions play a very important role in carbonylation reaction because they provide another route for carbonylated products especially when the migratory insertion of CO is difficult. For example, adequate basic conditions facilitate the nucleophilic attack of alkoxide on ligand CO and make it possible to carry out the catalytic carbonylation of allyl halides under atmospheric pressure of CO (see **1-4-1** in this chapter).[18b)]

1-2-3. Oxidative Addition of Organic Acyl Compounds.

Among catalytic reactions of this kind, hydroacylation,[10)] hydroesterification,[11)] and hydroamidation[12)] are known as C-C bond-forming reactions using formyl compounds such as aldehyde, formate ester, and formamide, respectively (**Scheme 1.9**). In the proposed mechanism, these formyl compounds react with a low-valent metal to give hydride-acyl metal complexes. The insertion of olefins into the metal-hydrogen bond and the subsequent reductive elimination give two carbon extended ketones, esters, or amides (see notes).



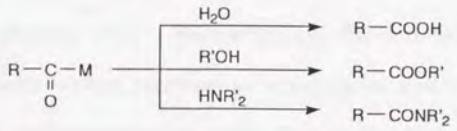
Scheme 1.9 A possible mechanism for hydroacylation hydroesterification, and hydroamidation.
Y = Alkyl, Aryl, OR, NR_2

Although not catalytic and rarely used as a synthetic method for organic compounds, reactions of acyl halides with low-valent metals are useful for the synthesis of acyl complexes which can be model intermediates of catalytic reactions. Sometimes it is possible to obtain complexes which are hardly synthesized by normal CO insertion reactions. For example, α-ketoacyl palladium or platinum complexes can be synthesized by using α-ketoacid halides.[13a,b] These complexes are characterized for the mechanistic study of the double carbonylation reaction of organic halides reported by Yamamoto[13] and Tanaka[14] groups.

1-3. Reaction of Acyl-Metal Intermediates.

Although the most simple reaction of acyl-metal complexes is decarbonylation which is sometimes used as a synthetic method, this is the reverse reaction of the (migratory) CO insertion and not documented here. The following classification is neither precise nor exact one because sometimes it is difficult to distinguish which kind of reaction is actually occurring, especially from mechanistic point of view. Therefore, the author wish to classify here the reaction of acyl-metal complexes according to the reactant which the complexes react with.

1-3-1. Reaction with Nucleophiles.

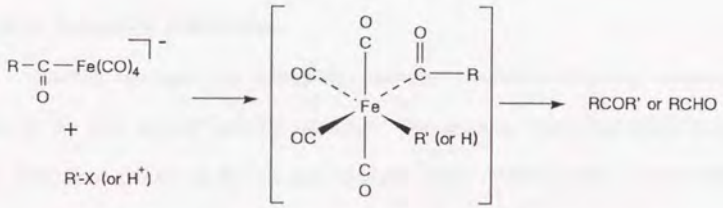


Scheme 1.10 Reaction of acyl complex with nucleophiles.

Reactions of this kind are known well and often the final step of catalytic carbonylations where products are released from metal (**Scheme 1.10**). The mechanism may be different, and depend on the nucleophiles and acyl complexes. But unfortunately, few has been reported as a systematic study for the reaction mechanism.

1-3-2. Reaction with Electrophiles.

As low-valent metal complexes react with electrophiles, anionic acyl complexes readily react with various electrophiles, typically organic halides or trialkyloxonium salts. For these complexes to react with nucleophiles, normally the addition of an oxidant is necessary. Acyl complexes can no longer stay anionic in such conditions.

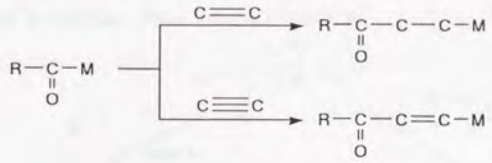


Scheme 1.11 Synthesis of Ketone or Aldehyde by Collman's Reagent.

When an alkyl nucleophile reacts on a metal center of an acyl-complex, the subsequent reductive elimination from the resulting alkyl acyl complex gives a ketone. This reaction is considered to be involved in the ketone synthesis by Collman's reagent referred earlier (**Scheme 1.11**).[6] Electrophiles can also react with on the oxygen in an acyl ligand. Fischer-carbene complexes are often isolated after treatment of the anionic complexes with trialkyloxonium salt which leads to the O-alkylation of the carbene ligand.

1-3-3. Insertion of Alkenes and Alkynes.

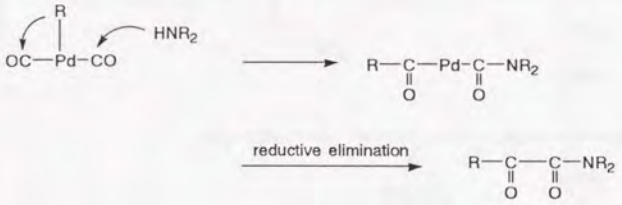
As an unsaturated compound, alkenes can coordinate to metals and insert into metal-H or metal-C bonds. Although the mechanisms of the olefin insertions for some systems are still a matter of controversy, the fact that olefins do insert into acyl-metal bonds is well-known as an "acyl-metalation" and utilized for organic synthesis (**Scheme 1.12**). Typical examples are described in Chapter 6.



Scheme 1.12 Acylmetalation reactions.

1-3-4. Reductive Elimination.

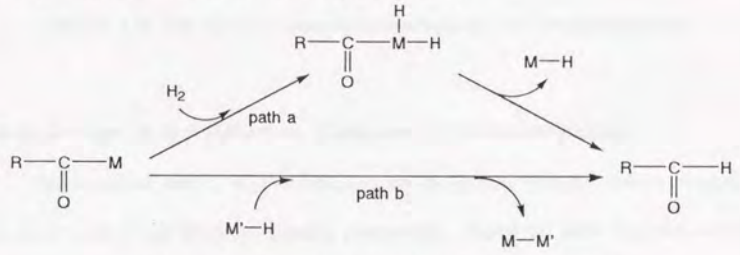
Besides reactions with nucleophiles, reductive elimination from acyl complexes can also be the final step of catalytic reactions. The resulting low-valent metal complexes are often good precursors for the next catalytic cycle. When another moiety which the acyl group will bind with is also an acyl group, the elimination affords α-ketocarbonyl compounds. The double-carbonylation affording α-keto amides referred earlier is believed to involve such a mechanism (**Scheme 1.13**). In this reaction, the carbamoyl group is thought to be generated by the nucleophilic attack of an amine on the ligand CO.



Scheme 1.13 Mechanism for the palladium catalyzed double-carbonylation.

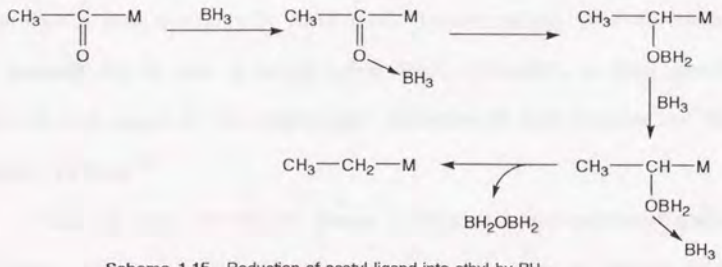
1-3-5. Reaction with Hydrogen or Metal-Hydride.

One reaction of this kind is the formation of an aldehyde, which is closely related to the hydroformylation (oxo reaction).[15] When H_2 oxidatively adds to an acyl complex, reductive elimination from the resulting complex leads to the formation of an aldehyde (**Scheme 1.14, path a**). Another mechanism is proposed for Co catalyst system which involves the reaction of an acyl complex with a hydride complex to give an aldehyde and a dinuclear cobalt complex (**path b**).



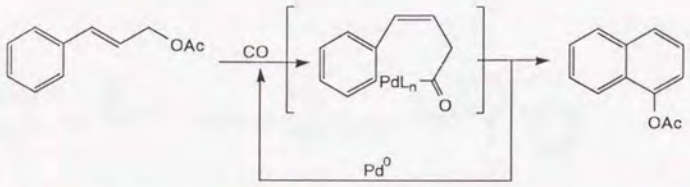
Scheme 1.14 Formation of aldehyde form acyl-metal complex.

Another reaction of this kind is the reduction of an acyl ligand. For example, a BH_3·THF adduct is reported to reduce acetyl into ethyl ligand for various metal complexes (**Scheme 1.15**).[16] These reactions provide a possible pathway involved in the Fischer–Tropsch reaction where linear hydrocarbons are selectively formed from CO and H_2.



Scheme 1.15 Reduction of acetyl ligand into ethyl by BH_3.
M = Fe, Ru, Ir, Pt, Pd, Co, and Mo

1-4. Palladium or Platinum Catalyzed Cyclocarbonylation of Cinnamyl Compounds Affording 1-Naphthol Derivatives.

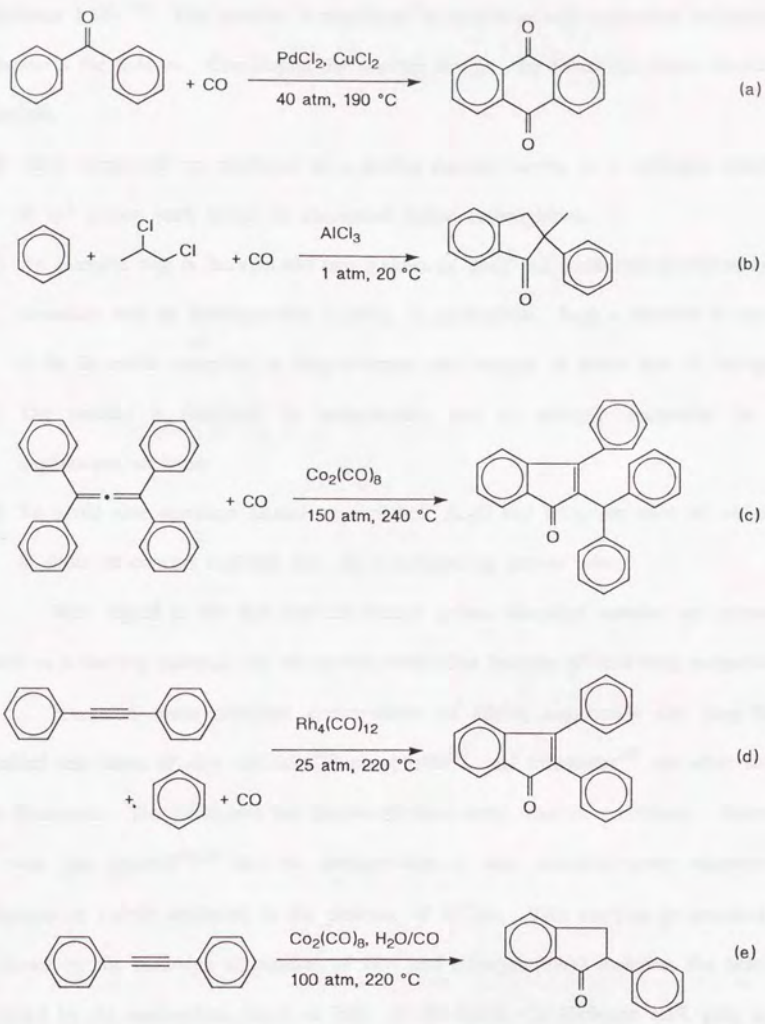


Scheme 1.16 The Palladium Catalyzed Cyclocarbonylation of Cinnamyl Compounds.

1-4-1. Design of the Palladium Catalyzed Cyclocarbonylation.

As described above, acyl complexes can be formed through various routes, and they react with many kinds of organic compounds. Some of their reactions are quite similar to those of acid halides which are also known to react with nucleophiles such as water, alcohol, or amine to give carboxylic acids, esters, or amides, respectively, or with olefins to give ketones. It is also well-known that acid halides react with aromatic rings to give aryl ketones in the presence of a Lewis acid, that is, the Friedel-Crafts acylation. If acyl complexes are regard as analogue of acid halides, they are also expected to react with an aromatic ring to give aryl ketones. But a few reactions are known which seem to involve the direct reaction between an acyl-metal intermediate and an aromatic ring to form a carbon-carbon bond. Moreover, so little generality is observed with regard to their application. Examples of such reactions are listed in **Scheme 1.17a-e**.[17)]

From this point of view, Dr. Koyasu designed and developed novel synthesis of 1-naphthol derivatives by palladium-catalyzed cyclocarbonylation of cinnamyl compounds


PdCl2, CuCl2
40 atm, 190 °C
+ CO
(a)
AlCl3
1 atm, 20 °C
Cl
Cl
+ CO
(b)
Co2(CO)8
150 atm, 240 °C
+ CO
(c)
Rh4(CO)12
25 atm, 220 °C
+ CO
(d)
Co2(CO)8, H2O/CO
100 atm, 220 °C
(e)

Scheme 1.17

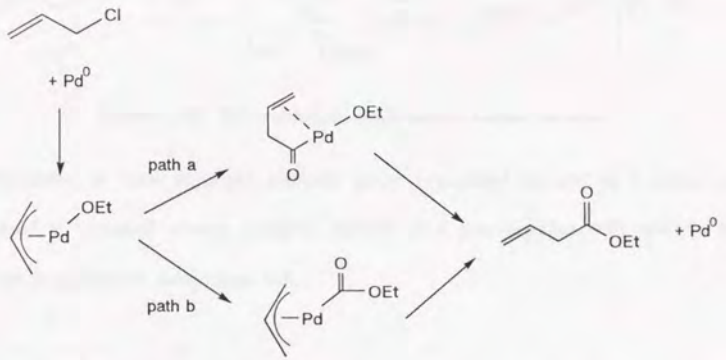
(**Scheme 1.16**).[23a] This reaction is considered to involve an acyl-palladium intermediate shown in the Scheme. Considering the reaction design, the following points should be noticed.

1) Allyl compounds are employed as a starting material having no β-hydrogen attached to sp^3 carbon such would be eliminated before carbonylation.
2) An aromatic ring is incorporated into a substrate itself that turns carbon-carbon bond formation into an intramolecular reaction i.e. cyclization. Such a reaction is known to be favorable compared to intermolecular one because of lower loss of entropy.
3) The product is stabilized by isomerization into an aromatic compound i.e. an naphthalene skeleton.
4) To avoid side reactions caused by naphthol, Ac_2O and NEt_3 are used as additives in order to convert naphthol into the corresponding acetate ester.

With regard to the first and the second points, cinnamyl acetates are normally used as a starting materials for the cyclocarbonylation because of their easy preparation.

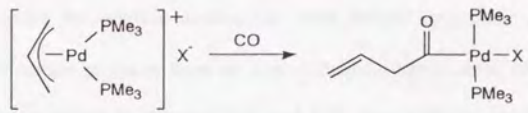
Transition metal-catalyzed carbonylation of allylic compounds has long been studied and those of allyl chlorides[18], phosphates[19], and carbonates[20] are often found in literatures. The latter two are known for their mild reaction conditions. Recently it was also reported[18a,b] that the carbonylation of allyl chlorides under atmospheric pressure of CO is attainable in the presence of EtONa. This reaction is proposed to proceed by the reductive elimination of allyl and ethoxycarbonyl moieties; the latter is formed by the nucleophilic attack of EtO^- on the ligand CO (**Scheme 1.18**, path a).

The reason for the difficulty to carbonylate allyl compounds under mild conditions is mainly attributed to the high stability of π-allyl complexes which hardly undergo migratory CO insertion. Recently Yamamoto *et al.* reported[21] that PMe_3-coordinated



Scheme 1.18 Palladium Catalyzed Carbonylationof Allyl Chloride.

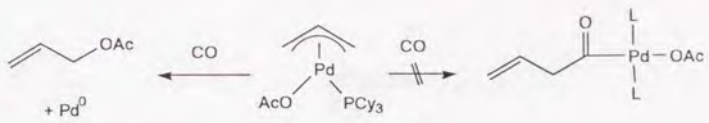
cationic π–allyl palladium complexes undergo CO insertion to give 3–butenoylpalladium complexes (**Scheme 1.19**). This report indicates that the CO insertion into palladium–π–allyl bond is a kinetically feasible process.



Scheme 1.19 CO Insertion of π-Allylpalladium Complex.

With regard to the combination of allyl acetates and palladium complexes, the addition of CO to the system containing π–allyl palladium acetate complexes is reported not to result in the CO insertion but in the reductive elimination regenerating the starting allyl acetate (**Scheme 1.20**).[22] Murahashi *et al.* reported[19b] that the addition of bromide anion facilitates the palladium catalyzed carbonylation of allyl acetates under mild conditions although the reason for the effect is not clear yet.

Although the effect of leaving groups are not examined in detail for the cyclo–



Scheme 1.20 Carbonylation of π-Allylpalladium Acetate Complex.

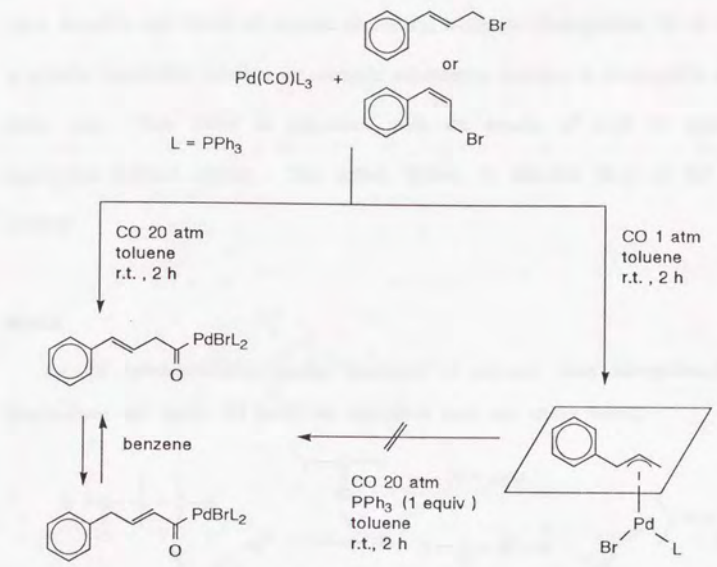
carbonylation, at least cinnamyl bromide gives 1-naphthyl acetate in a lower yield compared to cinnamyl acetate, possibly because of a side reaction with additive NEt_3 to form a quaternary ammonium salt.

1-4-2. Starting Point of This Work.

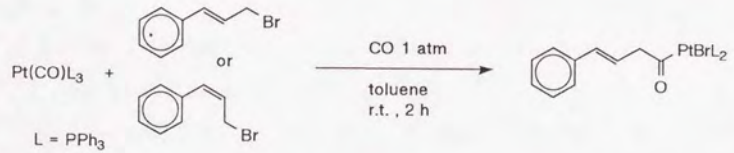
As application of this cyclocarbonylation for organic synthesis, only reported is the synthesis of simply substituted naphthalenes.[23a,c] It is uncertain whether the cyclocarbonylation is applicable to the synthesis of further polycyclic compounds or fused heteroaromatic compounds.

Concerning the reaction mechanism, most interest is focused on the step where C-C bond formation proceeds from an acyl-palladium intermediate on cyclization. The model complexes shown in **Scheme 1.21** and **1.22** were prepared by Dr. Matsuzaka and they did afford 1-naphthyl acetate under catalytic reaction conditions.[23b,c] The spectroscopic analyses of these complexes were expected to show the interaction between the acyl-metal moiety and the aromatic ring. But unfortunately they took *E*-form with regard to C=C double bond which made the phenyl ring and the metal so separated while, as is readily understood, they have to isomerize into *Z*-form for cyclization. As the result, it was very difficult to obtain further information for cyclization step from these complexes.

As other approaches to understand the cyclization step, the comparison of relative



Scheme 1.21 Preparation of Model Complexes for the Palladium Catalyzed Cyclocarbonylation.

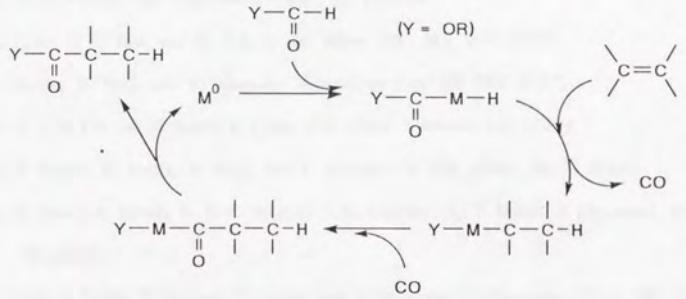


Scheme 1.22 Preparation of Model Complexes for the Palladium Catalyzed Cyclocarbonylation; Platinum Analogue.

reactivity and the check of the cyclization selectivity are expected to be useful. As is often found in text books of organic chemistry, it can be distinguished by its orientation or relative reactivities whether an aromatic substitution reaction is electrophilic or nucleophilic one. This thesis is concerned with the results of such an approach and application referred earlier. The author wishes to describe them in the following chapters.

Notes

For the hydroesterification, another mechanism is proposed where alkoxycarbonyl group is decarbonylated and another CO inserts into alkyl-metal bond (see scheme below).



References for Chapter 1.

1) R. H. Crabtree in "*The Organometallic Chemistry of the Transition Metals*", John-Wiley & Sons, pp. 62-64 (1988).

2) F. Calderazzo, *Angew. Chem., Int. Ed. Engl.*, **16**, 299 (1977).

3) S. B. Butts, S. H. Strauss, E. M. Holt, R. E. Stimson, N. W. Alcock, and D. F. Shriver, *J. Am. Chem. Soc.*, **102**, 5093 (1980).

4) F. Ozawa and A. Yamamoto, *Chem. Lett.*, 289 (1981).

5) N. Koga and K. Morokuma, *J. Am. Chem. Soc.*, **108**, 6136 (1986).

6) J. P. Collman, *Acc. Chem. Res.*, **8**, 342 (1975).

7) P. J. Fagan, K. G. Moloy, and T. J. Marks, *J. Am. Chem. Soc.*, **103**, 6959 (1981).

8) a) R. J. Angelici, *Acc. Chem. Res.*, **5**, 335 (1972).

   b) E. O. Fischer, *Adv. Organomet. Chem.*, **14**, 1 (1976).

9) N. Grice, S. C. Kao, and R. Petit, *J. Am. Chem. Soc.*, **101**, 1627 (1979).

10) T. Kondo, Y. Tsuji, and Y. Watanabe, *Tetrahedron Lett.*, **28**, 6229 (1987).

11) a) I. J. B. Lin and H. Alper, *J. Chem. Soc., Chem. Commun.*, 248 (1989).

   b) T. Kondo, S. Yoshii, Y. Tsuji, and Y. Watanabe, *J. Mol. Catal.*, **50**, 31 (1989).

   c) P. Isnard, B. Denise, R. P. A. Sneeden, J. M. Cognion, and P. Durual, *J. Organomet. Chem.*, **256**, 135 (1983).

12) Y. Tsuji, S. Yoshii, T. Ohsumi, T. Kondo, and Y. Watanabe, *J. Organomet. Chem.*, **331**, 379 (1987).

13) a) F. Ozawa, N. Kawasaki, H. Okamoto, T. Yamamoto, and A. Yamamoto, *Organometallics*, **6**, 1640 (1987).

   b) F. Ozawa, H. Soyama, H. Yanagihara, I. Aoyama, H. Takino, K. Izawa, T. Yamamoto, and A. Yamamoto, *J. Am. Chem. Soc.*, **107**, 3235 (1985).

   c) F. Ozawa, H. Soyama, T. Yamamoto, and A. Yamamoto, *Tetrahedron Lett.*, **23**, 3383 (1982).

14) a) T. Kobayashi and M. Tanaka, *J. Organomet. Chem.*, **233**, C64 (1982).

   b) M. Tanaka, T. Kobayashi, and T. Sakakura *J. Chem. Soc., Chem. Commun.*, 837 (1985).

15) a) B. Cornils in "*New Syntheses with Carbon Monoxide*"; J. Falbe, Ed.; Springer-Verlag: Berlin, 1980; p 1.

b) I. Tkatchenko in "*Comprehensive Organometallic Chemistry*"; G. Wilkinson, F. G. A. Stone, E. W. Abel, Eds.; Pergamon: New York, 1982; Vol.8 , p 101.

16) J. A. V. Doorn, C. Masters, H. C. Volger, *J. Organomet. Chem.*, **105**, 245 (1976).

17) a) G. G. Arzoumanidis and F. C. Rauch, *J. Mol. Catal.*, **9**, 335 (1980).

b) H. A. Bruson and H. L. Plant, *J. Org. Chem.*, **32**, 3356 (1967).

c) P. J. Kim and N. Hagihara, *Bull. Chem. Soc. Jpn.*, **38**, 2022 (1965).

d) P. Hong, B. Cho, and H. Yamazaki, *Chem. Lett.*, 339 (1979).

e) K. Doyama, K. Fujiwara, T. Joh, K. Maeshima, and S. Takahashi, *Chem. Lett.*, 901 (1988).

18) a) J. Kiji, T. Okano, W. Nishiumi, and H. Konishi, *Chem. Lett*, 957 (1988).

b) J. Kiji, T. Okano, H. Konishi, and W. Nishiumi, *36th Symposium on Organometallic Chemistry, Japan*, abstract PB106, (1989).

c) F. Joó and H. Alper, *Organometallics*, **4**, 1775 (1985).

d) W. T. Dent, R. Long, and G. H. Whitfield, *J. Chem. Soc.*, 1588 (1964).

e) J. Tsuji, J. Kiji, S. Imamura, and M. Morikawa, *J. Am. Chem. Soc.*, **86**, 4350 (1964).

19) a) S. Murahashi and Y. Imada, *Chem. Lett.*, 1477 (1985).

b) S. Murahashi, Y. Imada, Y. Taniguchi, and S. Higashiura, *Tetrahedron Lett.*, **29**, 1477 (1985).

20) a) J. Tsuji, K. Sato, and H. Okumoto, *J. Org. Chem.*, **49**, 1341 (1984).

b) J. Tsuji, K. Sato, and H. Okumoto, *Tetrahedron Lett.*, **23**, 5189 (1982).

21) F. Ozawa, T. Son, K. Osakada, and A. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1067 (1989).

22) a) Y. Takahashi, K. Tsukiyama, S. Sakai, and Y. Ishii, *Tetrahedron Lett.*, 1913 (1970).

b) T. Yamamoto, O. Saito, and A. Yamamoto, *J. Am. Chem. Soc.*, **103**, 5600 (1981).

23) a) Y. Koyasu, H. Matsuzaka, Y. Hiroe, Y. Uchida, and M. Hidai, *J. Chem. Soc., Chem. Commun.*, 575 (1987).

b) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *Chem. Lett.*, 377 (1988).

c) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *J.Org.Chem.*, **53**, 3832 (1988).

Chapter 2

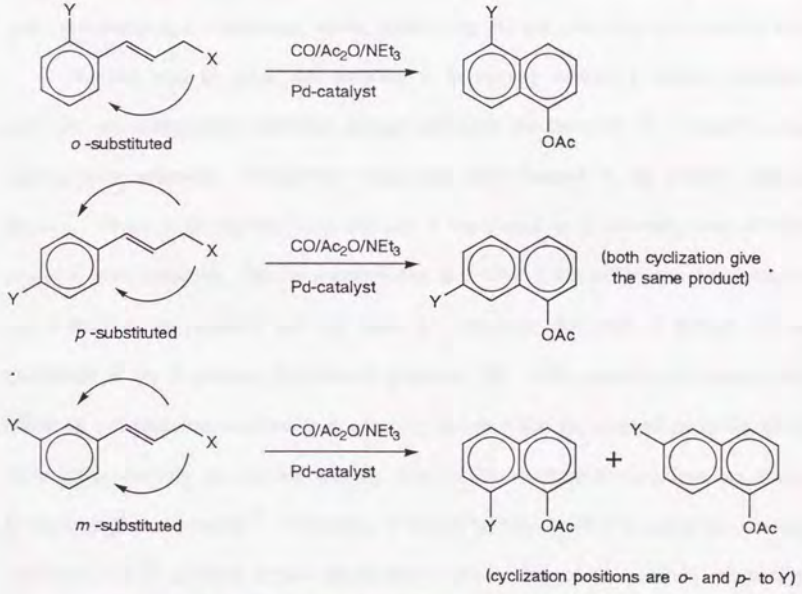
Highly Selective Synthesis of Phenanthryl Acetates by Palladium-Catalyzed Cyclocarbonylation of 3-(Naphthyl)allyl Acetates

Abstract

Phenanthryl acetates were obtained in good yields by the carbonylation of 3-(naphthyl)allyl acetates in the presence of Ac_2O, NEt_3, and a catalytic amount of palladium-phosphine complexes in benzene solution under CO pressure at 160 °C. The cyclocarbonylation of 3-(2-naphthyl)allyl acetates affords 4-phenanthryl acetates selectively by the cyclization at the 1-position of the naphthalene nucleus.

2-1. Introduction.

As mentioned in Chapter 1, the cyclocarbonylation of simple cinnamyl compounds has already been reported.[1] As far as mono-substituted phenyl compound was employed as a substrate, it could not be distinguished from its orientation whether the cyclization step of the reaction is electrophilic or nucleophilic one by nature (**Scheme 2.1**). When *o*- or *p*-substituted cinnamyl compound was used, there was only one possible product. When *m*-substituted substrate was used, there were two possible products but the positions where annulation occurred were the *o*- and *p*-positions to the substituent and the product distribution did not reflect the electronic character of the

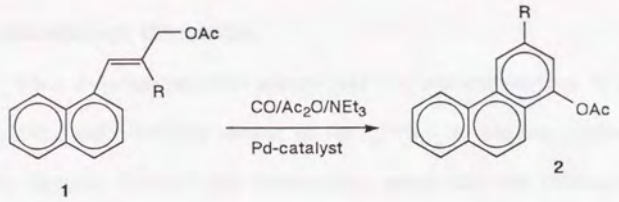


Scheme 2.1 Cyclocarbonylation of monosubstituted cinnamyl acetates. (X = OAc)

cyclization step. For example,[1b] the cyclocarbonylation of *m*-methylcinnamyl acetate gave 6-methyl- and 8-methylnaphthyl acetate in the ratio of 42:58 (total 69 % yield). This ratio is not so informative because, in electrophilic substitution reactions of toluene, the *o/p* products ratio (or partial rate factors) varies in a very wide range depending on reactants and conditions.[2]

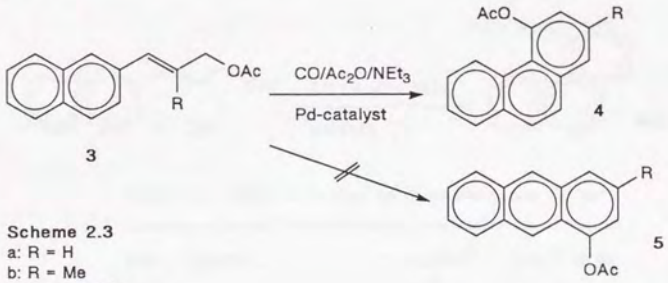
One possible solution for this problem is to compare the relative reaction rate using substrates having different substituents. But this attempt was unsuccessful because each substrate gave the corresponding product at almost the same rate even in the competitive reaction where two substrates were allowed to react in one vessel at the same time.[1b] A possible explanation for this result is that the cyclization step is not rate-determining and substituents on the phenyl ring did not affect the total reaction rate.

Another way to solve this problem is to employ substrates whose cyclization positions are electronically different enough to reflect the character of cyclization step. Among such substrates, 2-naphthyl compounds were seemed to be suitable for the purpose. When 3-(2-naphthyl)allyl acetates **3** were used as a substrate, two different products were expected. One is phenanthrene derivative **4** formed by the cyclization at the 1-position (α-position) and the other is anthracene derivative **5** formed by the cyclization at the 3-position (β-position) (**Scheme 2.3**). With regard to an electrophilic attack on a naphthalene nucleus, it is generally accepted that the α-position is kinetically more active than the β-position, that is, most of the electrophilic reactions are known to occur at the α-position.[3] Therefore, it would be very helpful to know the products distribution of 2-naphthyl system for further understanding of the reaction mechanism, although steric factors must also be considered. In this chapter, the author wishes to describe the results on these studies.



1 2

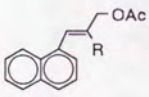
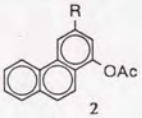
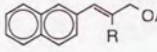
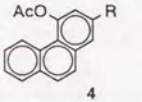
Scheme 2.2
a: R = H
b: R = Me



3 4 5

Scheme 2.3
a: R = H
b: R = Me
c: R = CH_2OAc

Table 2.1 Synthesis of Phenanthrenes from γ-(Naphthyl)ally Acetates.

Entry	Substrate	R	Product	Reaction Time / h	Isolated Yield / %
1		H		1.5	50
2		CH_3		3	70
	1		2		
3		H		1.5	73
4		CH_3		3	76
5		CH_2OAc		3	50
	3		4		

Reaction conditions:

Substrate 3 mmol	CO 70 atm at room temp.
$PdCl_2(PPh_3)_2$ 0.15 mmol	170 °C
Ac_2O 6 mmol	
NEt_3 6 mmol	
benzene 2 mL	

2-2. Results and Discussion.

When 3-(1-naphthyl)allyl acetate (**1a**) was cyclocarbonylated in the presence of Ac_2O, NEt_3, and a catalytic amount of $PdCl_2(PPh_3)_2$ in benzene, cyclization at the β-position smoothly occurred and 1-phenanthryl acetate (**2a**) was obtained in 50 % yield from the reaction mixture (**Scheme 2.2** and **Table 2.1**). On the other hand, the cyclocarbonylation of 3-(2-naphthyl)allyl acetate (**3a**) gave 4-phenanthryl acetate (**4a**)

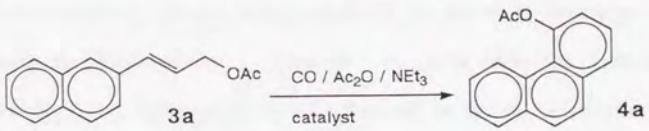


Table 2.2 Effect of Catalyst on Cyclocarbonylation of **3a**.*

Run	Catalyst	Conversion[a] / %	Yield[a] of **4a** / %
1	$PdCl_2(PPh_3)_2$	98	80
2	$PdCl_2(PMePh_2)_2$	99	43
3	$PdCl_2(PMe_2Ph)_2$	98	58
4	$PdCl_2(PMe_3)_2$	90	57
5	$PdCl_2(PCy_3)_2$	93	27
6[b]	$PdCl_2(PCy_3)_2$	91	74
7	$PdCl_2(P(OPh)_3)_2$	3	3
8	$PtCl_2(PPh_3)_2$	22	16
9	$RhCl(PPh_3)_3$	<1	trace
10	$Ru_3(CO)_{12}$ + $3PPh_3$	<1	trace
11	$Co_2(CO)_8$	<1	trace

Reaction conditions: **3a** 3 mmol, catalyst 0.03 mg atom of metal, Ac_2O 6 mmol, NEt_3 6 mmol, benzene 2 mL, CO 50 kg/cm^2 at room temperature, 160 °C, 1 h.

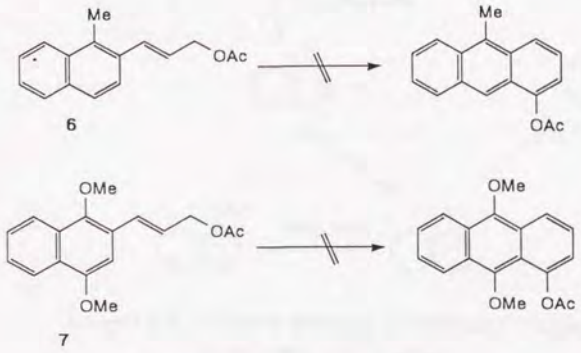
* In every run, **5a** was not detected in the reaction mixture.

a) Based on **3a**, determined by GLC.

b) Reaction temperture 195 °C.

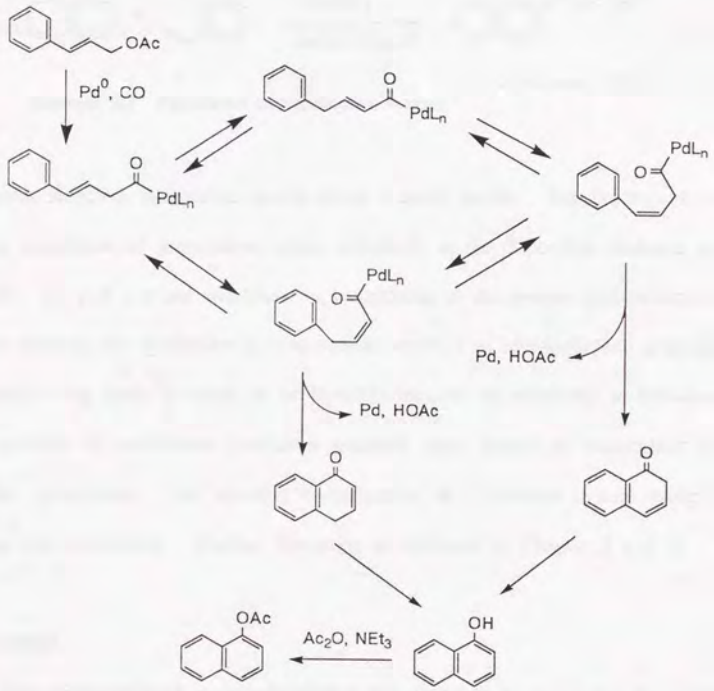
selectively in 73 % yield and anthracene derivative **5a** was not detected in the reaction mixture (**Scheme 2.4**). **4a** was identified by its melting point and ^{1}H NMR signal at δ 9.10 which shifted to rather low field as an aromatic proton and was characteristic for 4- and 5-protons of phenanthrene derivatives (See Experimental). The absence of 1-anthryl acetate (**5a**) was confirmed by comparison of the gas chromatogram of the reaction mixture with that of an authentic sample of **5a** prepared by a literature method. It was also confirmed that the absence of **5a** is not due to its instability under high temperature reaction conditions. When **5a** was placed under the catalytic reaction conditions for 1.5 h, GLC analysis showed that most of **5a** (86 %) stayed unreacted in the resulting reaction mixture.

The selectivity was not affected by phosphine ligands of Pd-catalyst (**Table 2.2**, Run 1-7), reaction temperature (Run 6), nor metal of catalyst complexes (Run 9-11). The high selectivity for α-cyclization was also shown by catalytic reactions of substrates whose α-position was blocked by methyl (**6**) or methoxy group (**7**) (**Scheme 2.4**). They were completely consumed after 3 h but only high-boiling oily products were obtained and no anthracene derivative was detected from the reaction mixture by GLC.

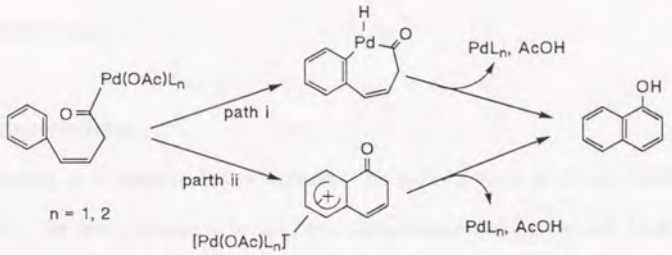


Scheme 2.4 Cyclocarbonylation of 1-blocked 3-(2-naphthyl)allyl acetates.

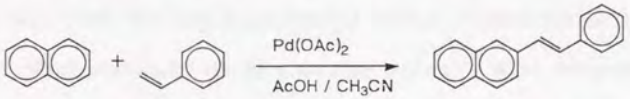
Based on the stoichiometric reaction of model complexes, a mechanism for the cyclocarbonylation has already been proposed[1b,4] which involves the cyclization from $[(Z\text{-}PhCH{=}CHCH_2CO)Pd(OAc)(PPh_3)_n]$ or $[(Z\text{-}PhCH_2CH{=}CHCO)Pd(OAc)(PPh_3)_n]$ to produce a cyclic ketone. The subsequent isomerization and acetylation of the ketone would afford the final product (**Scheme 2.5**). At present the mechanistic detail on the cyclization step is not clear. One possible pathway is the formation of a metalacycle from the acyl–Pd(II) complex by (ortho–)palladation (**Scheme 2.6**, path i). The



Scheme 2.5 Proposed Mechanism of Pd-Catalyzed Cyclocarbonylation
L = OAc, PPh_3, CO n = 2 - 4



Scheme 2.6 Possible Mechanisms for the Cyclization Step.



Y.Fujiwara (1975)

Scheme 2.7 Palladation on Naphthalene Nucleus.

subsequent reductive elimination would afford a cyclic ketone. But Fujiwara reported that the palladation of naphthalene occurs selectively at the β-position (**Scheme 2.7**).[5] Therefore, the path i is not considered to be included in the present cyclocarbonylation. Another pathway, the cyclization by electrophilic attack of an acyl-palladium intermediate on aromatic ring (path ii) seems to be plausible because, as mentioned in Introduction, the α-position of naphthalene nucleus is generally more subject to electrophilic attack than the β-position. The selective α-cyclization of 2-naphthyl system found here suggests this mechanism. (Further discussion is described in Chapter 3 and 4)

Conclusion

Palladium-catalyzed cyclocarbonylation was found to be useful for the synthesis of substituted phenanthrenes which are hardly obtained by traditional substitution reactions of phenanthrene or the Haworth synthesis. The α-cyclization of 2-naphthyl system

suggested the cyclization step of the cyclocarbonylation to be an electrophilic attack on an aromatic ring.

2-3. Experimental.

Preparation of 3-(naphthyl)allyl acetates. All solvents were dried and distilled under nitrogen. **1a** was prepared according to a literature method.[5] **3c** was kindly offered from Dr. Y.Ishii. **1b**, **3a**, and **3b** were prepared from the corresponding naphthaldehyde by three steps. The first step is condensation between aldehyde and ethyl acetate or propionate, which was carried out by a literature method.[7] When aldehyde was solid, it was dissolved in THF or the reactant ester itself. The resulting α,β-unsaturated ester was reduced by $LiAlH_4$ at -20 °C or *iso*-Bu_2AlH at room temperature to give allylic alcohol. The acetylation of the alcohol was achieved by mixing it with Ac_2O, NEt_3, and small amount (ca. 1 %) of *p*-dimethylaminopyridine (DMAP) in ether solution and stirring at room temperature for 12-20 h. The mixture was washed with 1N aq HCl, 10 % aq $NaHCO_3$, and water, then dried over Na_2SO_4 or $MgSO_4$. Solvent was evaporated and residual crude product was purified either by recrystallization or distillation in vacuo. Characterization data are as follows.

3-(1-Naphthyl)-2-methylallyl acetate (1b). Colorless oil. b.p. 116-126 °C/0.1 mmhg. ^{1}H NMR δ 1.75 (s, 3H, vinyl-CH_3, 2.17 (s, 3H, $COCH_3$), 4.78 (s, 2H, CH_2), 6.75 (s, 1H, vinyl), 7.33 (d, *J* = 7.0 Hz, 1H, Ar), 7.44-7.51 (m, 3H, Ar), 7.78 (d, *J* = 7.8 Hz, 1H, Ar), 7.84-7.94 (m, 2H, Ar).

3-(2-Naphthyl)allyl acetate (3a). Recrystallization from hexane gave white powder. ^{1}H NMR δ 2.12 (s, 3H, $COCH_3$), 4.78 (d, *J* = 6.4 Hz, 2H, CH_2), 6.41 (dt, *J* = 15.9, 6.4 Hz, 1H, vinyl), 6.81 (d, *J* = 15.9 Hz, 1H, vinyl), 7.43-7.49 (m, 2H, Ar), 7.59 (dd,

J = 1.7, 8.6 Hz, 1H, Ar), 7.75 (s, 1H, Ar), 7.78–7.81 (m, 3H, Ar).

3-(2-Naphthyl)-2-methylallyl acetate (3b). Pale yellow oil. b.p. 118–128 °C/0.1 mmHg. Gradually solidified at room temperature. ^{1}H NMR δ 1.98(d, J = 1.2 Hz, 3H, vinyl-CH_3, 2.15 (s, 3H, $COCH_3$), 4.69 (d, J = 1.2 Hz, 2H, CH_2), 6.68(s, 1H, vinyl), 7.36–7.50 (m, 3H, Ar), 7.73 (s, 1H, Ar), 7.79–7.83(m, 3H, Ar).

3-(1-Methyl-2-naphthyl)allyl acetate (6). Yellow oil. Method for the preparation of **1a** was applied.* Treatment of Grignard reagent prepared from 2-bromo-1-methyl-naphthalene[8] and magnesium with acrolein in ether and usual work up gave 1-(1-methyl-2-naphthyl)allyl alcohol. An Ac_2O solution of the alcohol was boiled under reflux for 6 h. After removing excess Ac_2O by distillation, residual oil was chromatographed on silica gel to give **6** as an yellow oil. ^{1}H NMR δ 2.12 (s, 3H, $COCH_3$), 2.67 (s, 3H, Ar-CH_3), 4.80 (d, J = 6.5 Hz, 2H, CH_2), 6.25 (dt, J = 6.5, 15.8 Hz, 1H, vinyl), 7.18 (d, J = 15.8 Hz, 1H, vinyl), 7.43–7.53 (m, 2H, Ar), 7.57 (d, J = 7.6 Hz, 1H, Ar), 7.66 (d, J = 8.5 Hz, 1H, Ar), 7.79 (d, J = 8.7 Hz, 1H, Ar), 8.06 (d, J = 8.5 Hz, 1H, Ar).

3-(1,4-Dimethoxy-2-naphthyl)allyl acetate (7). A mixture of 2-bromo-1,4-dimethoxy-naphthalene[8] (11 g, 41 mmol), methyl acrylate (4.5 g, 52 mmol), $Pd(OAc)_2$ (92.4 mg, 0.04 mmol), tri(o-tolyl)phosphine (626 mg, 2.06 mmol), and NEt_3 (50 mL) was stirred at 100 °C for 20 h. The mixture was diluted with ether up to 200 mL, washed with water, dil.HCl, 10 % aq $NaHCO_3$, and again with water, then was dried over $MgSO_4$. Evaporation of solvent gave black oil which gradually solidified. Purification by silica gel column chromatography (hexane/$CHCl_3$/EtOAc, 12:6:1) and recrystallization (hexane) gave methyl 3-(1,4-dimethoxy-2-naphthyl)acrylate as grayish green needles (7.8 g, 28

---

* The method employed for the preparation of **7** is recommended.

mmol). ^{1}H NMR δ 3.85 (s, 3H, OMe), 3.94 (s, 3H, OMe), 4.01 (s, 3H, OMe), 6.52 (d, J = 16.2 Hz, 1H, vinyl), 6.86 (s, 1H, 3-naphthyl), 7.51-7.58 (m, 2H, Ar), 8.10 (d, J = 7.9 Hz, 1H, Ar), 8.19-8.23 (m, 2H, vinyl and Ar). Reduction of the ester by $LiAlH_4$ and usual work up gave 3-(1,4-Dimethoxy-2-naphthyl)allylalcohol as yellow blocks. Acetylation of the alcohol gave **7** (79 % from the unsaturated ester). Recrystallization from hexane gave pale yellow needles. ^{1}H NMR δ 2.13 (s, 3H, $COCH_3$), 3.88 (s, 3H, OMe), 4.00 (s, 3H, OMe), 4,83 (dd, J = 1.2, 6.4 Hz, 2H, CH_2), 6.38 (dt, J = 6.4, 16.1 Hz, 1H, vinyl), 6.86 (s, 1H, 3-naphthyl), 7.18 (dt, J = 1.2, 16.1 Hz, 1H, vinyl), 7.44-7.55 (m, 2H, Ar), 8.06 (d, J = 7.6 Hz, 1H, Ar), 8.20 (d, J = 7.6 Hz, 1H, Ar).

General Procedure for Cyclocarbonylation of 3-(Naphthyl)allyl Acetates. The following procedure is representative. A mixture of **1a** (3 mmol), $PdCl_2(PPh_3)_2$ (0.15 mmol), Ac_2O (6 mmol), NEt_3 (6 mmol), and benzene (2 mL) in a stainless steel autoclave was pressurized with CO (70 kg/cm^2 at room temperature) and was heated at 170 °C for 1.5 h with stirring. Then the autoclave was cooled and CO was discharged. The mixture was diluted with ether, was washed (1N Hcl, 10 % aq $NaHCO_3$, and water), and dried ($MgSO_4$). Solvent was evaporated and crude product was purified by silica gel column chromatography (1,2-dichloroethane/hexane, 1:1) and recrystallization (hexane) to give **2a** in 50 % yield.

Reaction conditions of the attempted cyclocarbonylation of **6** and **7** are the same as described in **Table 2.1** with reaction time 3 h. Blank reaction of **5a** was carried out under the following conditions; **5a** 0.25 mmol, $PdCl_2(PPh_3)_2$ 0.0125 mmol, Ac_2O 0.5 mmol, NEt_3 0.55 mmol, benzene 0.5 mL, CO 50 kg/cm^2 at room temp., 160 °C, 1.5 h. Naphthalene was added to the resulting mixture as internal standard and the mixture

was analyzed by GLC.

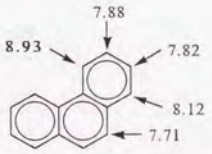
1-Phenanthryl acetate (2a). Colorless needles. mp. 137–140 °C. ^{1}H NMR δ 2.42 (s, 3H, $COCH_3$), 7.30 (dd, J = 1.1, 7.7 Hz, 1H, Ar), 7.53–7.62 (m, 3H, Ar), 7.72 (AB, J = 9.5 Hz, 2H, Ar), 7.83 (dd, J = 1.3, 7.7 Hz, 1H, Ar), 8.53 (d, J = 8.5 Hz, 1H, Ar), 8.60 (d, J = 8.2 Hz, 1H, Ar). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found C, 81.20; H, 5.16.

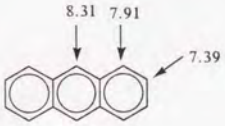
3-Methyl-1-phenanthryl acetate (2b). Colorless blocks from hexane. mp. 105–107 °C. ^{1}H NMR δ 2.48 (s, 3H, $COCH_3$), 2.61 (s, 3H, Ar-CH_3), 7.20 (s, 1H, Ar), 7.57–7.66 (m, 2H, Ar), 7.72 (AB, J = 9.3 Hz, 2H, Ar), 7.87 (dd, J = 1.3, 7.8 Hz, 1H, Ar), 8.38 (s, 1H, Ar), 8.65 (d, J = 7.9 Hz, 1H, Ar). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found C, 81.83; H, 5.67.

4-Phenanthryl acetate (4a). Purified by silica gel column chromatography (1,2-dichloroethane/hexane, 1:1) and recrystallization (hexane). Colorless blocks. mp. 60.3–61.5 °C (lit.[10] 58–60 °C). ^{1}H NMR δ 2.55 (s, 3H, $COCH_3$), 7.33 (dd, J = 1.2, 7.6 Hz, 1H, Ar), 7.56–7.65 (m, 3H, Ar), 7.73 (AA', 2H, Ar), 7.81 (dd, J = 1.2, 7.9 Hz, 1H, Ar), 7.89 (dd, J = 2.1, 6.6 Hz, 1H, Ar), 9.10 (dd, J = 2.1, 7.3 Hz, 1H, 5-H of phenanthrene nucleus (see notes in this page)). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found C, 81.26; H, 5.10.

---

cf. δ Values (^{1}H NMR) of phenanthrene and anthracene.





2-Methyl-4-phenanthryl acetate (4b). Colorless blocks from hexane. mp. 113-114 °C. ^{1}H NMR δ 2.54 (s, 3H, $COCH_3$), 2.61 (s, 3H, Ar-CH_3), 7.17 (d, J = 1.8 Hz, 1H, Ar), 7.55-7.63 (m, 3H, Ar), 7.67 (AB pattern, J = 8.9 Hz, 2H, Ar), 8.87 (dd, J = 1.8, 7.3 Hz, 1H, Ar), 9.03 (dd, J = 1.2, 8.3 Hz, 1H, Ar) . Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found C, 81.54; H, 5.73.

2-Acetoxymethyl-4-phenanthryl acetate (4c). Colorless blocks. ^{1}H NMR δ 2.15 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 5.30 (s, 2H, CH_2), 7.33 (d, *J* = 1.8 Hz, 1H, Ar), 7.58-7.65 (m, 2H, Ar), 7.73 (AB, *J* = 8.9 Hz, 2H, Ar), 7.78 (d, *J* = 1.8 Hz, 1H, Ar), 7.88-7.90 (m, 1H, Ar), 9.07 (d, *J* = 8.2 Hz, 1H, Ar).

1-Anthryl acetate (5a). Prepared by literature procedures.[11] 9,10-Anthraquinone-1-sulfonic acid sodium salt was commercially obtained as the starting material. Colorless needles from hexane. mp. 134.1-135.7 °C (lit.[12] 129-130 °C). ^{1}H NMR δ 2.55 (s, 3H, $COCH_3$), 7.25 (d, *J* = 7.3 Hz, 1H, Ar), 7.42-7.50 (m, 3H, Ar), 7.91 (dd, *J* = 0.6, 8.5 Hz, 1H, Ar), 7.99-8.03 (m, 2H, Ar), 8.43 (s, 1H, Ar), 8.47(s, 1H, Ar).

References and Notes for Chapter 2.

1) a) Y. Koyasu, H. Matsuzaka, Y. Hiroe, Y. Uchida, and M. Hidai, *J. Chem. Soc., Chem. Commun.*, 575 (1987).

b) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *J. Org. Chem.*, **53**, 3832 (1988).

2) Several reported data for the electrophilic substitution of toluene are summarized in the **Table 2.3**.

Table 2.3

Reaction	Reagents	Partial rate factors		
		o_f	m_f	p_f
Nitration	$HNO_3(CH_3NO_2)$	38.9	1.3	45.7
Chlorination	$Cl_2(AcOH)$	617	5	820
Bromination	$Br_2((AcOH-H_2O)$	600	5.5	2420
Benzoylation	$PhCOCl(AlCl_3,\ PhNO_2)$	32.6	5.0	831
Acetylation	$AcCl(AlCl_3,\ ClCH_2CH_2Cl)$	4.5	4.8	749
Benzylation	$PhCH_2Cl(AlCl_3)$	4.2	0.4	10.0
Methylation	$CH_3Br(GaBr_3)$	9.5	1.7	11.8

3) Two typical exceptions which include the substitution at the β-position are the sulfonation at high temperatures and the acylation with $AlCl_3$ in nitrobenzene. The former is a reversible reaction and the β-selectivity is explained by thermodynamic reasons. That of the latter is due to the steric hindrance of a bulky reactant formed from an acid chloride, $AlCl_3$, and nitrobenzene. Like many acylation reactions, the present cyclocarbonylation is considered to be irreversible and controlled kinetically. With regard to steric factors, the α-selectivity of the present reaction indicates that they are not operative, which is also discussed in the Chapter 4.

4) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *Chem. Lett.*, 377 (1988).

5) Y. Fujiwara, R. Asano, I. Moritani, and S. Teranishi, *Chem. Lett.*, 1061 (1975).

6) H. Burton, *J. Chem. Soc.*, 759 (1931).

7) C. S. Marvel and W. B. King, *Org. Syn., Coll. Vol. 1*, 252 (1967).

8) W. E. Parham, H. E. Reiff, and P. Swartzentruber, *J. Am. Chem. Soc.*, **78**, 1437 (1956).

9) H. Uno, *J. Org. Chem.*, **51**, 350 (1986).

10) H. M. Duvall and E. Mosettig, *J. Am. Chem. Soc.*, **60**, 2409 (1938).

11) a) R. E. Schmit, *Chem. Ber.*, **37**, 66 (1904).

b) H. Dienel, *Chem. Ber.*, **38**, 2862 (1905).

12) H. E. Frietz-David, L. Blangey, and H. Streiff, *Helv. Chim. Acta*, **29**, 1718 (1946).

Chapter 3

Palladium–Catalyzed Cyclocarbonylation of 3–(Heteroaryl)allyl Acetates

Abstract

Acetoxybenzofurans, acetoxybenzothiophenes, acetoxyindoles, and acetoxycarbazoles were obtained in high yields by the cyclocarbonylation of 3–furyl–, 3–thienyl–, 3–pyrrolyl–, and 3–indolylallyl acetates, respectively, in the presence of Ac_2O, NEt_3, and a catalytic amount of $PdCl_2(PPh_3)_2$ at 130–170 °C under 50–70 atm of CO. 3–(3–Furyl)allyl and 3–(3–thienyl)allyl acetates cyclized selectively at the 2–position of the heterocyclic nucleus to give 7–acetoxybenzofuran and 7–acetoxybenzothiophene, respectively. The synthetic utility of the reaction was demonstrated by the synthesis of cannabifuran from isothymol.

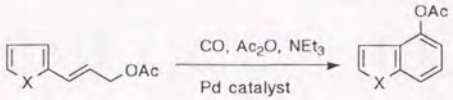
3-1. Introduction.

As mentioned in Chapter 1, the palladium-catalyzed cyclocarbonylation had not been applied to the synthesis of heterocyclic compounds when the author started his work. Fused heteroaromatics such as benzofuran, benzothiophene, indole, and carbazole are among the most attractive groups of compounds as targets in organic synthesis because of their wide occurrence in natural products. Especially desirable is the development of a selective synthetic route for fused heteroaromatics having functional groups at specific positions. In their respect, cyclocarbonylation of heteroaromatic compounds seems to be promising. Although there have been a few reports dealing with a catalytic cyclocarbonylation (see Chapter 1, **1-4-1**), no such reaction of heteroaromatic substrates has appeared in a literature. The cyclocarbonylation is synthetically advantageous in that substrates of cinnamyl acetate type is easily accessible. Similar cyclocarbonylation of 3-(heteroaryl)allyl acetates was expected to afford various fused heteroaromatic compounds having an acetoxy group. In this chapter, the author wish to describe the results of this approach in detail.

3-2. Results and Discussion.

The cyclocarbonylation of various 3-(heteroaryl)allyl acetates was catalyzed by $PdCl_2(PPh_3)_2$. NEt_3 and Ac_2O were used to esterify, *in situ*, phenols initially produced. Reaction temperatures above 130 °C were necessary to obtain high (> 80 %) yields. Therefore, most of the reactions were performed at 170 °C. At lower temperatures, lower yields were obtained. Side reactions at lower temperatures afforded unidentifiable high-boiling by-products. For example, at 100 °C, **1a** gave **2a** in only 48% yield, although **1a** was completely consumed (**Table 3.3**, Run 3).

3-2-1. Synthesis of Benzofurans and Benzothiophenes.



(1)

X = O, S

As shown in **Table 3.1** and **Eq (1)**, cyclocarbonylation of 3-(furyl)allyl acetates and 3-(thienyl)allyl acetates gave acetoxybenzofurans and acetoxybenzothiophenes, respectively, in high yields. Only with **1b**, a secondary allylic acetate, no cyclo-carbonylation product was isolated. In this case, elimination of acetic acid and polymerization of the resulting diene were, possibly, competing reactions.[1] The γ-substituted allyl acetate **1d** gave acetoxybenzofuran **2d**, but the yield was relatively low (**Table 3.1**, Run 4). Here also, diene formation and subsequent polymerization probably occurred. The secondary allylic alcohol **3** also gave **2a** in moderate yield (Run 7). Here, acetylation apparently preceded carbonylation.* The dibenzofuran skeleton was also constructed from 3-(2-benzofuranyl)allyl acetate (**7**) (Run 10). It is of great interest that 3-(3-furyl)allyl acetate (**4a**) and 3-(3-thienyl)allyl acetate (**4b**) selectively cyclized at the 2-position of the heterocyclic nucleus to give 7-acetoxybenzofuran (**5a**) and 7-acetoxybenzothiophene (**5b**), respectively, as the only products (Run 8,9). No 3-acetoxyisobenzofuran (**6a**), 3-acetoxyisobenzothiophene (**6b**), or related compounds formed by cyclization at the 4-position of the heterocyclic nucleus were detected (**Scheme 3.1**).

---

* 1-Phenylallyl alcohol was also cyclocarbonylated to 1-naphthyl acetate in 45 % yield (isolated).

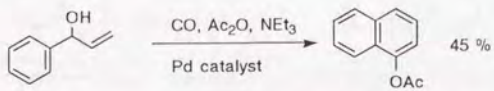
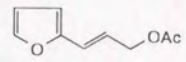
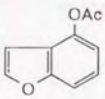
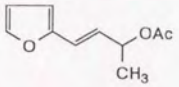
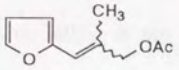
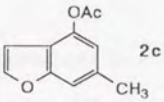
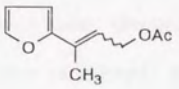
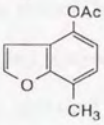
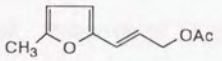
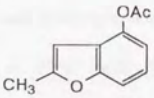
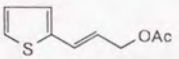
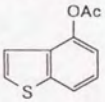
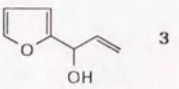
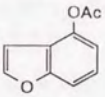
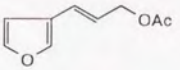
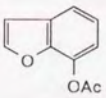
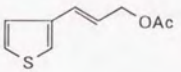
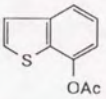
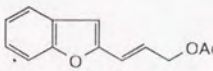
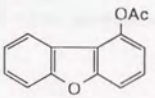
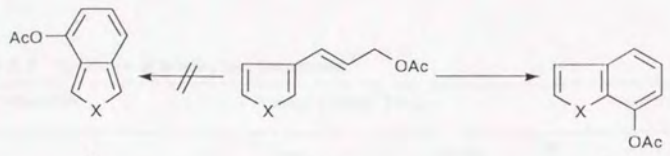


Table 3.1 Synthesis of Benzofurans and Benzothiophenes.

Run	Substrate	Product	Isolated Yield / %
1	 **1a**	 **2a**	85
2	 **1b**	———	
3	 **1c**	 **2c**	78
4	 **1d**	 **2d**	56
5	 **1e**	 **2e**	76
6	 **1f**	 **2f**	79
7	 **3**	 **2a**	56
8	 **4a**	 **5a**	89
9	 **4b**	 **5b**	86
10	 **7**	 **8**	70

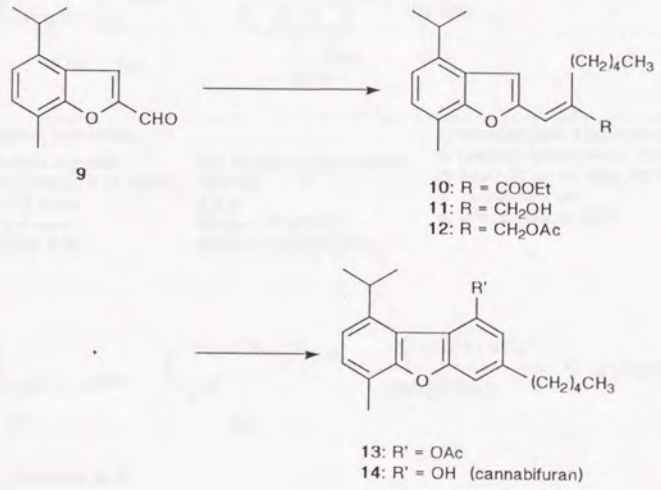
Typical reaction conditions: substrate 3 mmol, $PdCl_2(PPh_3)_2$ 0.15 mmol, Ac_2O 6 mmol, NEt_3 6 mmol, benzene 2 ml, CO 60 atm at room temp., 170 °C, 1.5 h.



6 4 5

Scheme 3.1
a: X = O
b: X = S

The synthetic utility of the reaction was demonstrated in a facile synthesis of cannabifuran (**14**), a naturally occurring dibenzofuran derived from *Cannabis sativa* L.[2] Benzofuran **12** was easily obtained by reduction and subsequent acetylation of the condensation product of aldehyde **9** (prepared from isothymol[3]) and ethyl heptanoate. Cyclocarbonylation of **12** proceeded smoothly, and acetoxydibenzofuran **13** was obtained in 74% yield. Hydrolysis of **13** afforded **14** in 94% yield (**Scheme 3.2**).



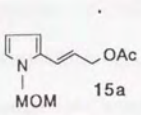
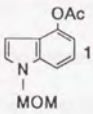
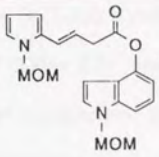
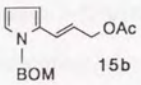
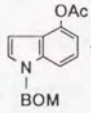
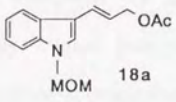
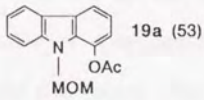
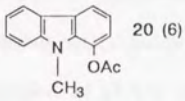
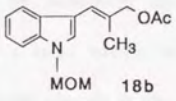
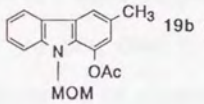
9

10: R = COOEt
11: R = CH_2OH
12: R = CH_2OAc

13: R' = OAc
14: R' = OH (cannabifuran)

Scheme 3.2 Synthesis of Cannabifuran.

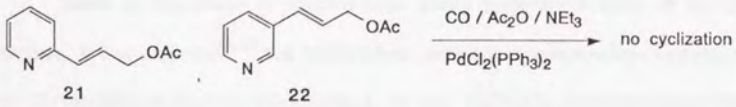
Table 3.2 Synthesis of Indoles and Carbazoles.[a]

Run	Substrate	Product (Yield[b] / %)			
1	 15a	 16a	(52)	 17	(28)
2[c]			(57)		(trace)
3[d]			(52,69[e])		(6)
4	 15b	 16b	(36)		
5	 18a	 19a	(53)	 20	(6)
6	 18b	 19b	(36)		

a) Reaction conditions:

Substrate 3 mmol	CO 70 atm at room temp.
$PdCl_2(PPh_3)_2$ 0.15 mmol	130 °C
Ac_2O 6 mmol	1.5 h
NEt_3 6 mmol	MOM = $-CH_2OCH_3$
benzene 2 mL	BOM = $-CH_2OCH_2Ph$

b) Isolated yield based on substrate.
c) reaction temperature 170 °C.
d) Ac_2O 12 mmol, NEt_3 12 mmol, benzene 4 mL.
e) Determined by GLC.



Scheme 3.3

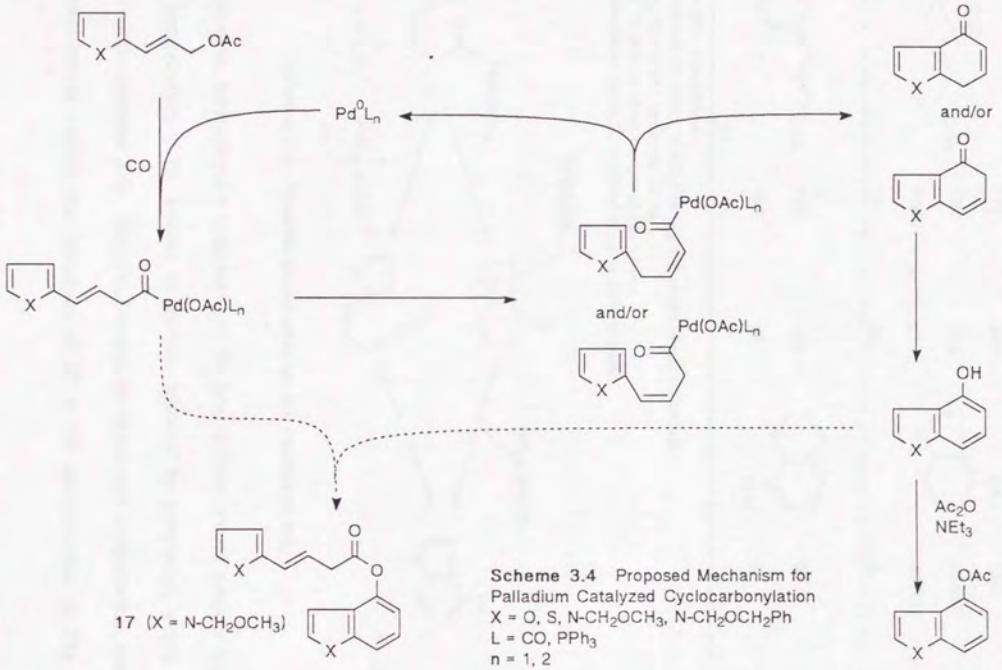
3-2-2. Synthesis of Indoles and Carbazoles.

Allyl acetates substituted with a pyrrole or indole ring underwent cyclocarbonylation at 130 °C. Thus, 3-(2-pyrrolyl)- and 3-(3-indolyl)allyl acetates gave 4-acetoxyindoles and 1-acetoxycarbazoles, respectively (**Table 3.2**). However, the yields were somewhat lower than those obtained from furan or thiophene systems, probably because of the relative instability of five-membered nitrogen heterocycles.[4] On the other hand, 3-(2-pyridyl)- and 3-(3-pyridyl)allyl acetates (**21** and **22**, respectively) gave *no* cyclocarbonylation products, even at 170 °C (**Scheme 3.3**).

Compound **15a** gave not only **16a** but also dimeric **17**. Compound **17** was possibly formed from the reaction of 4-hydroxy-1-(methoxymethyl)indole and an intermediate acylpalladium complex (*vide infra*). The formation of **17** was suppressed either by performing the reaction at a higher temperature (**Table 3.2**, Run 2), or by using a large excess of Ac_2O and NEt_3 (Run 3). In both cases, there was no significant change in the yield of **16a**. In the cyclocarbonylation of **18a**, in addition to the expected product **19a**, a small amount of the N-methylcarbazole **20** was obtained. The mechanism of the formation of this by-product is not clear.

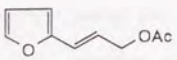
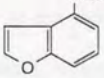
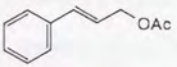
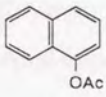
3-2-3. The Reaction Mechanisms.

Based on the results of stoichiometric model cyclocarbonylation of the cinnamyl acetates, it was proposed[6a,b] that intermediate unsaturated acylpalladium complexes, such as $[(Z)\text{-ArCH=CHCH}_2\text{CO}]\text{Pd(OAc)(PPh}_3)_n$ or $[(Z)\text{-ArCH}_2\text{CH=CHCO}]\text{Pd(OAc)(PPh}_3)_n$ (n = 1 or 2), could be formed by successive oxidative addition of allylic acetate, CO insertion, and C=C double bond *E*-*Z* isomerization. It is reasonable to assume that similar intermediates are involved in the cyclocarbonylation of 3-(heteroaryl)allyl acetates.

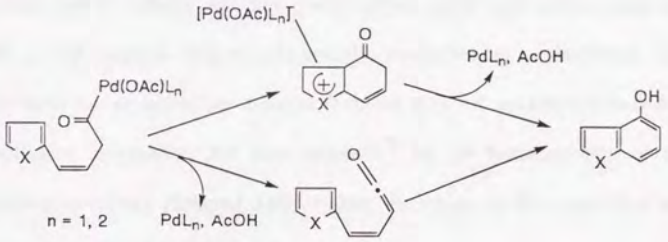


Scheme 3.4 Proposed Mechanism for Palladium Catalyzed Cyclocarbonylation
X = O, S, N-CH_2OCH_3, N-CH_2OCH_2Ph
L = CO, PPh_3
n = 1, 2

Table 3.3 Effect of Reaction Temperature: Relative Reactivity of Furan and Benzene Ring in the Cyclocarbonylation*

Run	Substrate	Reaction Temperature / °C	Conv. /%	Product	Yield** / %
1		170	100		(85)
2		130	100		98(83)
3		100	97		48(41)
4		70	33		5
5		170	100		81
6		100	99		2

*Reaction conditions:
Substrate 10 mmol, $PdCl_2(PPh_3)_2$ 0.5 mmol, Ac_2O 20 mmol,
NEt_3 20 mmol, benzene 10 ml,
CO 70 atm at room temperature, 1.5 h.
**Determined by GLC, isolated yield in parentheses.

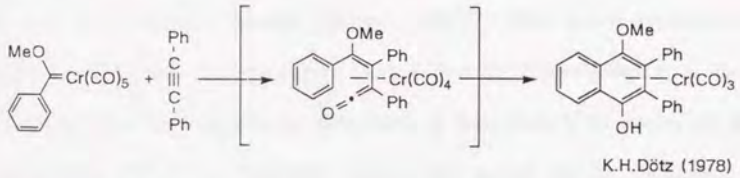


Scheme 3.5 Possible Mechanisms for the Cyclization Step.

In the latter case, intramolecular cyclization of the intermediates would produce bicyclic ketones. Isomerization of the ketones to phenols, followed by acetylation, would yield the final products (**Scheme 3.4**). Reaction between an unsaturated acylpalladium complex and a phenol would explain the formation of **17** in the carbonylation of **15a** (*vide supra*).

The detailed mechanism of the ring closure of the acyl complexes is still

unknown. However, several facts valuable in elaborating the mechanism were obtained. It was observed[6c] that the cyclization of 3-(2-naphthyl)allyl acetate occurred selectively at the 1-position of the aromatic nucleus, despite greater steric hindrance, to give 4-phenanthryl acetate (see Chapter 2, **Scheme 2.3**). In the reaction of 3-(heteroaryl)-allyl acetate, described above, **5a** and **5b** were similarly selectively formed, in good yields, from **4a** and **4b**, respectively. Furthermore, cinnamyl acetate gave 1-naphthyl acetate in only 2% yield (98% conversion) at 100 °C, whereas **1a** at 100 °C afforded **2a** in a moderate yield (**Table 3.3**). Finally, 3-(pyridyl)allyl acetates, **21** and **22** gave no cyclocarbonylation product even at 170 °C (*vide supra*). These facts indicate that the order of reactivity of aromatic rings in the cyclocarbonylation is furan > benzene > pyridine ring. Furthermore, the findings strongly suggest that the ring closure step is an electrophilic addition and may involve either direct electrophilic attack of the acyl moiety on the aromatic ring or, alternatively, cyclization of a vinylketene intermediate formed from the acylpalladium complex (**Scheme 3.5**). A reaction mechanism involving a vinylketene intermediate has been proposed[7] for the benzannulation of chromium-arylcarbene complexes (**Scheme 3.6**). Further discussion on the comparison of the both reactions is described in Chapter 4.



Scheme 3.6 Benzannulation Reaction of Arylcarbene-Chromium Complex with Alkyne

The present cyclocarbonylation requires rather drastic reaction temperature (160-

170 °C), and it is important to know which step is rate-determining. According to the **Scheme 3.4**, the catalytic cycle of the cyclocarbonylation consists of following step; (1) The oxidative addition of cinnamyl compound onto low-valent palladium complex. (2) The CO insertion into palladium-allyl bond. (3) The *E*/*Z* isomerization of allyl moiety. (4) The cyclization to form a cyclic ketone. (5) The isomerization of the ketone into a phenol. (6) The acetylation of the phenol. It is conceivable that the first two steps can proceed at lower temperatures because the starting material was consumed even at 100 °C (**Table 3.3**, Run 6), and a drop of CO pressure was observed after this reaction. In the Introduction of the Chapter 2, it was already mentioned that the fourth, cyclization step is not rate-determining at 160 °C. Evidently the fifth, isomerization step proceeds smoothly at much lower temperature because naphthols, having aromaticity, must be much more stable than naphthalenones. The final acetylation step can be carried out even at room temperature. Based on the discussion above, the third, *E*/*Z* isomerization step is considered to be rate-determining at present time.

This consideration is also supported by the fact that, even when *cis*-cinnamyl bromide was allowed to react with zero-valent palladium or platinum complexes under pressurized CO, the resulting butenoyl complexes were all *trans* with regard to C=C double bond (See Chapter 1, **Scheme 1.21** and **1.22**).[6b] These results are indicating that the *E*-configurations are much more favored than the *Z*-configurations in these systems. Therefore, the high reaction temperature is considered to be needed for the formation of the *Z*-butenoyl complexes quantitatively enough for the cyclization to proceed at sufficient rate to minimize side reactions.

Conclusion

In conclusion, palladium-catalyzed cyclocarbonylation was successfully applied to

the construction of fused-ring heteroaromatic compounds. The utility of the reaction as a synthetic tool was demonstrated by its use in the synthesis of cannabifuran. The relative reactivity and the cyclization selectivity suggested the cyclization step to be an electrophilic attack on an aromatic ring.

3-3. Experimental.

^1H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with a JEOL GX-400 spectrometer. $SiMe_4$ served as an internal standard. Fast atom bombardment mass spectra (FABMS) were recorded with a JEOL DX-300 instrument, using a *m*-nitrobenzylalcohol matrix. High resolution electron impact mass spectra (HREIMS) were recorded with a JEOL JMS AX-505H mass spectrometer. GLC analyses was performed with a Shimadzu GC-14A instrument equipped with a flame ionization detector and a 25 m Hicap-CBP1 capillary column. Helium was the carrier gas.

$PdCl_2(PPh_3)_2$ was prepared by a published method.[8] All solvents were dried, and then were distilled under nitrogen. With the exception of compounds **1a, 1b**, and **3**, the 3-substituted allyl acetates were prepared from the appropriate aromatic aldehyde in a manner similar to that used for the preparation of compound **7**. Unless indicated otherwise, Solid products were purified by recrystallization and oils were purified by Kugelrohr distillation.

3-(2-Furyl)allyl acetate (1a). To an ice-cooled solution of 3-(2-furyl)acrolein (5.01 g, 41 mmol) in MeOH (120 mL) was added $NaBH_4$ (2.3 g, 60 mmol) in small portions under N_2. The mixture was warmed to room temperature and stirred for 1 h. Evaporation of solvent gave a white slurry, which was dissolved in water (100 mL). The solution was extracted with ether. The extract was dried ($MgSO_4$). The solvent

was evaporated to give crude 3-(2-furyl)allyl alcohol (5.08 g, 100%) as a pale yellow oil. The crude alcohol was stirred with Ac_2O (5.7 mL), NEt_3 (11.2 mL), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (50 mg) in ether (100 mL) for 12 h at room temperature. The mixture was then washed (1 N aq HCl, saturated aq $NaHCO_3$, and water) and dried ($MgSO_4$). Solvent was evaporated to give crude **1a** as a yellow oil. Kugelrohr distillation gave a colorless oil (5.58 g, 33.6 mmol): ^{1}H NMR δ 2.08 (s, 3 H), 4.67 (dd, *J* = 1.4, 6.4 Hz, 2 H), 6.20 (dt, *J* = 16.0, 6.4 Hz, 1 H), 6.28 (d, *J* = 3.1 Hz, 1 H), 6.36 (dt, *J* = 1.8, 3.1 Hz, 1 H), 6.45 (dt, *J* = 16.0, 1.4 Hz, 1 H), 7.35 (d, *J* = 1.8 Hz, 1 H); IR (neat) 1745cm^{-1} (C=O). Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.88; H, 6.25.

3-(2-Furyl)-1-methylallyl acetate (1b). To a suspension of $LiAlH_4$ (4.0 g, 105 mmol) in THF (40 mL) at −20 °C was added, drop-by-drop, a solution of furfuralacetone (13.01g, 96 mmol) and THF (40 mL). The mixture was stirred at −20 to −10 °C for 3 h. Then the mixture was carefully hydrolyzed with 1 N aq HCl (100 mL). The two liquid layer was separated and the aqueous layer was extracted with ether several times. The combined organic layers were washed (saturated aq $NaHCO_3$ and water) and dried ($MgSO_4$). Evaporation of solvent gave 3-(2-furyl)-1-methylallyl alcohol as a pale yellow oil. The crude product was acetylated as described for **1a**. Distillation gave **1b** as a colorless oil (12.97 g, 68 % from furfuralacetone): bp 71-74 °C (0.5 mmHg); ^{1}H NMR δ 1.39 (d, *J* = 6.4 Hz, 3 H), 2.07 (s, 3 H), 5.48 (quintet of d, *J* = 6.6, 0.9 Hz, 1 H), 6.12 (dd, *J* = 6.6, 15.9 Hz, 1 H), 6.26 (d, *J* = 3.2 Hz, 1 H), 6.37 (dd, *J* = 1.8, 3.2 Hz, 1 H), 6.42 (dd, *J* = 0.9, 15.9 Hz, 1 H), 7.35 (d, *J* = 1.8 Hz, 1 H); IR (neat) 1735 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.52; H, 6.91.

3-(2-Furyl)-2-methylallyl acetate (1c). Colorless oil (24% from furfural): ^{1}H NMR δ 2.02 (d, *J* = 0.6 Hz, 3 H), 2.11 (s, 3 H), 4.60 (s, 2 H), 6.30-6.31 (m, 2 H), 6.41 (dd, *J* = 1.8, 3.3 Hz, 1 H), 7.39 (d, *J* = 1.8 Hz, 1 H); IR (neat) 1739 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.17; H, 6.58.

3-(2-Furyl)-3-methylallyl acetate (1d). Colorless oil (42% from 2-acetylfuran): ^{1}H NMR δ 2.00 (s, 3 H), 2.07 (s, 3 H), 4.77 (d, *J* = 7.3 Hz, 2 H), 6.16 (t, *J* = 7.3 Hz, 1 H), 6.32 (d, *J* = 3.4 Hz, 1 H), 6.37 (dd, *J* = 1.8, 3.4 Hz, 1 H), 7.35 (d, *J* = 1.8 Hz, 1 H); IR (neat) 1740 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.28; H, 6.87.

3-(5-Methyl-2-furyl)allyl acetate (1e). Colorless oil (39% from 5-methylfurfural): ^{1}H-NMR δ 2.08 (s, 3 H), 2.29 (s, 3 H), 4.68 (dd, *J* = 1.2, 6.7 Hz, 2 H), 5.96 (dq, *J* = 3.2, 0.9 Hz, 1 H), 6.13 (dt, *J* = 15.7, 6.7 Hz, 1 H), 6.16 (d, *J* = 3.2 Hz, 1 H), 6.39 (dt, *J* = 15.7, 1.2 Hz, 1 H); IR (neat) 1740 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 65.99; H, 6.72.

3-(2-Thienyl)allyl acetate (1f). Colorless oil (9% from 2-thiophenaldehyde): ^{1}H-NMR δ 2.07 (s, 3 H), 4.66 (d, *J* = 6.6 Hz, 2 H), 6.09 (dt, *J* = 15.5, 6.6 Hz, 1 H), 6.75 (d, *J* = 15.5 Hz, 1 H), 6.93-6.97 (m, 2 H), 7.15 (d, *J* = 5.2 Hz, 1 H); IR (neat) 1743 cm^{-1} (C=O). Anal. Calcd for $C_9H_{10}O_2S$: C, 59.32; H, 5.53. Found: C, 59.05; H, 5.71.

1-(2-Furyl)allyl alcohol (3). A 1 M solution of vinylmagnesium bromide in THF (37 mL) was added drop-by-drop to a solution of furfural (3.16 g) in ether (10 mL) at room temperature. The mixture was stirred for 3 h, then was hydrolyzed with saturated aq NH_4Cl (100 mL). The two liquid layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried ($MgSO_4$), and solvent was evaporated to give an orange oil. Purification by Kugelrohr distillation gave **3** (3.21 g)

as a colorless oil: ^{1}H NMR δ 4.55 (d, J = 5.5 Hz, 1 H, D_2O-exchangeable), 5.06–5.09 (m, 2 H), 5.27 (dt, J = 17.2 Hz, 1 H), 6.00 (ddd, J = 17.2, 10.1, 5.9 Hz, 1 H), 6.14 (dt, J = 3.1, 0.9 Hz, 1 H), 6.25 (dd, J = 3.1, 1.8 Hz, 1 H), 7.35 (dd, J = 1.8, 0.9 Hz, 1 H); IR (neat) 3320 cm^{-1} (OH). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.50; H, 6.72.

3-(3-Furyl)allyl acetate (4a). Colorless oil (46% from 3-furanaldehyde): ^{1}H NMR δ 2.09 (s, 3 H), 4.67 (dd, J = 1.2, 6.7 Hz, 2 H), 6.02 (dt, J = 15.9, 6.7 Hz, 1 H), 6.53 (m, 1 H), 6.53 (dt, J = 15.6, 1.2 Hz, 1 H), 7.37 (m, 1 H), 7.44 (s, 1 H); IR (neat) 1742 cm^{-1} (C=O). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.50; H, 6.72.

3-(3-Thienyl)allyl acetate (4b). Colorless oil (28% from 3-thiophenaldehyde): ^{1}H NMR δ 2.09 (s, 3 H), 4.69 (dd, J = 1.2, 6.4 Hz, 2 H), 6.14 (dt, J = 15.6, 6.4 Hz, 1 H), 6.66 (br d, J = 15.6 Hz, 1 H), 7.19–7.22 (m, 2 H), 7.28 (m, 1 H); IR (neat) 1735 cm^{-1} (C=O). Anal. Calcd for $C_9H_{10}O_2S$: C, 59.32; H, 5.53. Found: C, 59.63; H, 5.35.

3-(2-Benzofuranyl)allyl acetate (7). A solution of 2-benzofuranaldehyde (3.8 g, 26 mmol) in EtOAc(10 mL) was added drop-to-drop to a suspension of Na sand (0.80 g, 35 mmol) and absolute EtOH (0.1 mL) in EtOAc (10 mL) at −15 °C. The mixture was stirred for 2 h at −15 to −5 °C. AcOH (15 mL) and water (30 mL) were then carefully added. The two liquid layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed (saturated aq $NaHCO_3$ and water) and dried ($MgSO_4$). Solvent was evaporated to give crude ethyl 3-(2-benzofuranyl)acrylate as orange crystals (2.33 g, 10.7 mmol). The ester (2.33 g) was dissolved in toluene (30 mL), and diisobutylaluminium hydride (24 mmol) in toluene

(24 mL) was added drop-to-drop at 0 °C. The mixture was warmed to room temperature and stirred for 15 h. It was then hydrolyzed with 1 N aq HCl (50 mL), and the two liquid layers were separated. The aqueous layer was extracted with ether. The combined organic layers were washed (saturated aq $NaHCO_3$ and water) and dried ($MgSO_4$). The solvent was evaporated to give crude 3-(2-benzofuranyl)allyl alcohol as a yellow solid (1.76 g, 10.1 mmol). Acetylation as described above for **1a** gave **7** as a colorless solid (1.79 g, 8.3 mmol). Recrystallization (hexane/Et_2O, 95:5) gave colorless needles: mp 53-54 °C; ^{1}H NMR δ 2.12 (s, 3 H), 4.77 (d, *J* = 5.7 Hz, 2 H), 6.50 (dt, *J* = 15.6, 5.7 Hz, 1 H), 6.58 (d, *J* = 15.6 Hz, 1 H), 6.61 (s, 1 H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.27 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.43 (br d, *J* = 7.6 Hz, 1 H), 7.52 (br d, *J* = 7.6 Hz, 1 H); IR (KBr) 1738 cm^{-1} (C=O). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.10; H, 5.71.

3-(1-Methoxymethyl-2-pyrrolyl)allyl acetate (15a). Slightly red oil after purification by ice-cooled silica gel chromatography (ether/hexane, 1:2) (71% from *N*-methoxymethyl-2-pyrrolealdehyde): ^{1}H NMR δ 2.07 (s, 3 H), 3.23 (s, 3 H), 4.68 (dd, *J* = 1.2, 6.7 Hz, 2 H), 5.19 (s, 2 H), 6.09 (dt, *J* = 15.8, 6.7 Hz, 1 H), 6.13 (dd, *J* = 3.9, 2.7 Hz, 1 H), 6.43 (dd, *J* = 3.9, 1.7 Hz, 1 H), 6.63 (br d, *J* = 15.8 Hz, 1 H), 6.73 (dd, *J*·= 2.7, 1.7 Hz, 1 H); IR (neat) 1735 cm^{-1} (C=O). Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.17; H, 7.35; N, 6.95.

3-(1-Benzyloxymethyl-2-pyrrolyl)allyl acetate (15b). Pale yellow oil after purification by ice-cooled silica gel chromatography (ether/hexane, 1:2) (80% from *N*-benzyloxymethyl-2-pyrrolealdehyde): ^{1}H NMR (acetone-d_6) δ 2.06 (s, 3 H), 4.40 (s, 2 H), 5.26 (s, 2 H), 4.66 (d, *J* = 6.7 Hz, 2 H), 6.12 (dt, *J* = 15.7, 6.7 Hz, 1 H), 6.14 (dd, *J* = 3.7 2.8 Hz, 1 H), 6.45 (dd, *J* = 1.5, 3.7 Hz, 1 H), 6.64 (d, *J* = 15.7 Hz, 1 H), 6.71

(dd, J = 1.5, 2.8 Hz, 1 H), 7.27–7.36 (m, 5 H); ^{13}C-NMR (acetone-d_6) δ 21.3, 66.2, 70.6, 76.8, 109.7, 109.9, 122.2, 124.5, 125.1, 128.9, 129.0, 129.6, 132.0, 139.1, 171.2. IR (neat) 1738 cm^{-1} (C=O). HREIMS Calcd for $C_{17}H_{19}NO_3$: 285.137. Found: 285.138.

3-(1-Methoxymethyl-3-indolyl)allyl acetate (18a). Pale yellow oil after purification by ice-cooled silica gel chromatography (ether/hexane/benzene, 1:3:3) (12% from *N*-methoxymethyl-3-indolealdehyde): ^{1}H NMR δ 2.08 (s, 3 H), 3.19 (s, 3 H), 4.74 (d, J = 7.0 Hz, 2 H), 5.35 (s, 2 H), 6.29 (dt, J = 16.0, 7.0 Hz, 1 H), 6.80 (d, J = 16.0 Hz, 1 H), 7.16–7.27 (m, 3 H), 7.44 (d, J = 8.2 Hz, 1 H), 7.84 (d, J = 8.5 Hz, 1 H); IR (neat) 1732 cm^{-1} (C=O). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.59; H, 6.57; N, 5.02.

3-(1-Methoxymethyl-3-indolyl)-2-methylallyl acetate (18b). Pale yellow oil after purification by ice-cooled silica gel chromatography (ether/hexane:/benzene, 1:3:3) (53% from *N*-methoxymethyl-3-indolealdehyde): ^{1}H NMR δ 1.99 (s, 3 H), 2.13 (s, 3 H), 3.25 (s, 3 H), 4.72 (s, 2 H), 5.46 (s, 2 H), 6.71 (s, 1 H), 7.14–7.29 (m, 3 H), 7.47 (d, J = 8.2 Hz, 1 H), 7.66 (d, J = 7.9 Hz, 1 H); IR (neat) 1734 cm^{-1} (C=O). Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.53; H, 6.99; N, 5.11.

3-(2-Pyridyl)allyl acetate (21). Pale yellow oil after purification by silica gel chromatography (EtOAc/hexane/benzene, 2:2:1) (10% from 2-pyridinealdehyde). ^{1}H NMR (acetone-d_6) δ 1.99 (s, 3 H), 4.69 (dd, J = 1.5, 5.8 Hz, 2 H), 6.69 (dt, J = 15.7, 1.5 Hz, 1 H), 6.80 (dt, J = 15.7, 5.8 Hz, 1 H), 7.14 (dd, J = 4.6, 7.6 Hz, 1 H), 7.31 (d, J = 7.6 Hz, 1 H), 7.64 (t, J = 7.6 Hz, 1 H), 8.47 (d, J = 4.6 Hz, 1 H). ^{13}C NMR (acetone-d_6) δ 21.2, 65.1, 123.1, 123.8, 129.5, 133.6, 137.8, 150.9, 156.0, 171.1. HREIMS Calcd for $C_{10}H_{11}NO_2$: 177.079. Found: 177.080.

3-(3-Pyridyl)allyl acetate (22). Pale yellow oil after purification by silica gel

chromatography (EtOAc/hexane/benzene, 2:2:1) (18% from 3-pyridinealdehyde). ^{1}H NMR (acetone-d_6) δ 1.99 (s, 3 H), 4.66 (d, J = 6.1 Hz, 2 H), 6.41 (dt, J = 16.0, 6.1 Hz, 1 H), 6.65 (d, J = 16.0, 1 H), 7.25 (dd, J = 4.9, 8.1 Hz, 1 H), 7.79 (dt, J = 1.8, 8.1 Hz, 1 H), 8.40 (dd, J = 1.8, 4.9 Hz, 1 H), 8.58 (d, J = 1.8 Hz, 1 H). ^{13}C NMR (acetone-d_6) δ 21.2, 65.4, 124.7, 127.5, 130.8, 133.3, 134.0, 149.7, 150.2, 171.2. HREIMS Calcd for $C_{10}H_{11}NO_2$: 177.079. Found: 177.078.

Palladium-Catalyzed Cyclocarbonylation of 3-(Heteroaryl)allyl Acetates. The following procedure is representative. A mixture of **1a** (10 mmol), $PdCl_2(PPh_3)_2$ (0.5 mmol), Ac_2O (20 mmol), NEt_3 (20 mmol), and benzene (10 mL) in a stainless steel autoclave was pressurized with CO (70 kg/cm^2 at room temperature) and was heated at 170 °C for 1.5 h, with stirring. Then the autoclave was cooled and CO was discharged. The mixture was diluted with ether, was washed (dilute aq HCl, saturated aq $NaHCO_3$, and water) and dried ($MgSO_4$). Solvent was evaporated and the crude product was purified by silica gel column chromatography (1,2-dichloroethane/hexane, 1:2) to give 4-acetoxybenzofuran (**2a**) (85%) as a colorless oil. ^{1}H NMR δ 2.34 (s, 3 H), 6.65 (dd, J = 0.9, 2.1 Hz, 1 H), 6.99 (d, J = 8.2 Hz, 1 H), 7.26 (t, J = 8.1 Hz, 1 H), 7.38 (dd, J = 0.9, 8.2 Hz, 1 H), 7.57 (d, J = 2.1 Hz, 1 H); IR (neat) 1769 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 67.87; H, 4.56.

Additional amounts of Ac_2O (4 eq) and NEt_3 (4 eq) were used for the reactions of **3** and 1-phenylallyl alcohol.

4-Acetoxy-6-methylbenzofuran (2c). Colorless oil: ^{1}H NMR δ 2.37 (s, 3 H), 2.46 (s, 3 H), 6.61 (dd, J = 0.9, 2.1 Hz, 1 H), 6.83 (s, 1 H), 7.20 (d, J = 0.9 Hz, 1 H), 7.53 (d, J = 2.1 Hz, 1 H); IR (neat) 1764 cm^{-1} (C=O). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.91; H, 5.29.

4-Acetoxy-7-methylbenzofuran (2d). Colorless prisms (hexane): mp 49–50 °C; ^{1}H NMR δ 2.37 (s, 3 H), 2.50 (s, 3 H), 6.66 (d, *J* = 2.1 Hz, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 7.60 (d, *J* = 2.1 Hz, 1 H); IR (KBr) 1766 cm^{-1} (C=O). ^{13}C NMR δ 14.7, 20.9, 104.1, 115.1, 119.6, 120.4, 125.0, 141.8, 144.7, 154.9, 169.1. HREIMS Calcd for $C_{11}H_{10}O_3$: 190.063. Found: 190.061.

4-Acetoxy-2-methylbenzofuran (2e). Colorless prisms (hexane): mp 50–51 °C; ^{1}H NMR δ 2.36 (s, 3 H), 2.44 (d, *J* = 0.9 Hz, 3 H), 6.28 (m, 1 H), 6.92 (dd, *J* = 0.9, 8.1 Hz, 1 H), 7.18 (t, *J* = 8.1 Hz, 1 H), 7.29 (d, *J* = 8.1 Hz, 1 H); IR (KBr) 1764 cm^{-1} (C=O). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.37; H, 5.22.

4-Acetoxybenzothiophene (2f): Colorless needles (petroleum ether). mp 33–34 °C (lit.[9] 38.5–40.0 °C); ^{1}H NMR δ 2.41 (s, 3 H), 7.12 (dd, *J* = 0.9, 7.9 Hz, 1 H), 7.25 (dd, *J* = 0.9, 5.2 Hz, 1 H), 7.35 (t, *J* = 7.9 Hz, 1 H), 7.44 (d, *J* = 5.2 Hz, 1 H), 7.75 (dt, *J* = 0.9, 7.9 Hz, 1 H); IR (KBr) 1769 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_8O_2S$: C, 62.48; H, 4.20. Found: C, 62.84; H, 4.16.

7-Acetoxybenzofuran (5a). Colorless oil: ^{1}H NMR δ 2.41 (s, 3 H), 6.80 (d, *J* = 2.1 Hz, 1 H), 7.05 (dd, *J* = 7.9, 0.9 Hz, 1 H), 7.21 (t, *J* = 7.9 Hz, 1 H), 7.47 (dd, *J* = 0.9, 7.9 Hz, 1 H), 7.61 (d, *J* = 2.1, 1 H); IR (neat) 1771 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.53; H, 4.43.

7-Acetoxybenzothiophene (5b). Colorless oil: ^{1}H NMR δ 2.42 (s, 3 H), 7.15 (d, *J* = 7.9 Hz, 1 H), 7.35 (d, *J* = 5.4 Hz, 1 H), 7.37 (t, *J* = 7.9 Hz, 1 H), 7.43 (d, *J* = 5.4 Hz, 1 H), 7.69 (d, *J* = 7.9 Hz, 1 H); IR (neat) 1768 cm^{-1} (C=O). Anal. Calcd for $C_{10}H_8O_2S$: C, 62.48; H, 4.20. Found: C, 62.65; H, 4.16.

1-Acetoxydibenzofuran (8). Colorless prisms (hexane): mp 77–78 °C; ^{1}H NMR δ 2.50 (s, 3 H), 7.16 (dd, *J* = 6.1, 2.8 Hz, 1 H), 7.35 (ddd, *J* = 7.7, 7.3, 1.1 Hz, 1 H), 7.46

(d, J = 6.1 Hz, 1 H), 7.47 (d, J = 2.8 Hz, 2 H), 7.48 (ddd, J = 8.3, 7.3, 1.3 Hz, 1 H), 7.58 (ddd, J = 8.3, 1.1, 0.7 Hz, 1 H), 7.85 (ddd, J = 0.7, 1.3, 7.7 Hz, 1 H); IR (KBr) 1746 cm^{-1} (C=O). Anal. Calcd for $C_{14}H_{10}O_3$: C, 74.43; H, 4.46. Found: C, 74.17; H, 4.52.

4-Acetoxy-1-(methoxymethyl)indole (16a). Colorless prisms (hexane): mp 60–61 °C; ^1H NMR δ 2.83 (s, 3 H), 3.23 (s, 3 H), 5.42 (s, 2 H), 6.43 (d, J = 3.4 Hz, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 7.15 (d, J = 3.4 Hz, 1 H), 7.21 (t, J = 7.9 Hz, 1 H), 7.36 (d, J = 7.9 Hz, 1 H); IR (neat) 1764 cm^{-1} (C=O); FABMS m/e 219 (M^+). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.99; H, 6.00; N, 6.37.

4-Acetoxy-1-(benzyloxymethyl)indole (16b). Colorless prisms (hexane): mp 73–75 °C; ^1H NMR δ 2.39 (s, 3 H), 4.41 (s, 2 H), 5.52 (s, 2 H), 6.44 (d, J = 3.2 Hz, 1 H), 6.91 (d, J = 6.6 Hz, 1 H), 7.15 (d, J = 3.2 Hz, 1 H), 7.20–7.38 (m, 7 H); IR (KBr) 1759 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.46; H, 5.77; N, 4.60.

1-Methoxymethyl-4-[(*E*)-4-(1-methoxymethyl-2-pyrrolyl)-3-butenoyloxy]indole(17). Orange oil after purification by ice-cooled silica gel column chromatography (ether/hexane, 1:2): ^1H NMR δ 3.23 (s, 3 H), 3.25 (s, 3 H) 3.55 (dd, J = 1.5, 7.3 Hz, 2 H), 5.21 (s, 2 H), 5.42 (s, 2 H), 6.15 (t, J = 3.0 Hz, 2 H), 6.28 (dt, J = 15.9, 7.3 Hz, 1 H). 6.42 (d, J = 3.2 Hz, 1 H), 6.44 (dd, J = 3.0, 1.5 Hz, 1 H), 6.63 (br d, J = 15.9 Hz, 1 H), 6.73 (dd, J = 3.0, 1.5 Hz, 1 H), 6.92 (d, J = 8.1 Hz, 1 H) 7.14 (d, J = 3.2 Hz, 1 H), 7.21 (t, J = 8.1 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 1 H); IR (neat) 1756 cm^{-1} (C=O). HREIMS Calcd for $C_{20}H_{22}N_2O_4$: 354.158. Found: 354.159.

1-Acetoxy-9-(methoxymethyl)carbazole (19a). Colorless needles (benzene–hexane): mp 105–107 °C; ^1H NMR δ 2.41 (s, 3 H), 3.21 (s, 3 H), 5.77 (s, 2 H), 7.16 (dd, J =

1.0, 7.9 Hz, 1 H), 7.25 (t, J = 7.9 Hz, 1 H), 7.27 (ddd, J = 7.8, 6.7, 1.2 Hz, 1 H), 7.48 (ddd, J = 8.2, 6.7, 1.2 Hz, 1 H), 7.52 (br d, J = 8.2 Hz, 1 H), 7.95 (dd, J = 7.9, 1.0 Hz, 1 H), 8.06 (d, J = 7.6 Hz, 1 H); IR (KBr) 1765 cm^{-1} (C=O). FABMS *m/e* 269 (M^+). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.47; H, 5.71; N, 5.18.

1-Acetoxy-3-methyl-9-(methoxymethyl)carbazole (19b). Colorless needles (ether-hexane): mp 111-114 °C; ^1H NMR δ 2.41 (s, 3 H), 2.52 (s, 3 H), 3.19 (s, 3 H), 5.73 (s, 2 H), 6.99 (s, 1 H), 7.25 (t, J = 7.9 Hz, 1 H), 7.45 (t, J = 7.9 Hz, 1 H), 7.49 (d, J = 7.9 Hz, 1 H), 7.74 (s, 1 H), 8.02 (d, J = 7.9 Hz, 1 H); IR (KBr) 1769 cm^{-1} (C=O). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.11; H, 6.11; N, 4.95.

1-Acetoxy-9-methylcarbazole (20). Colorless needles (ether-hexane): mp 123-125 °C; ^1H NMR δ 2.44 (s, 3 H), 3.98 (s, 3 H), 7.14 (dd, J = 7.7, 1.4 Hz, 1 H), 7.18 (t, J = 7.7 Hz, 1 H) 7.24 (br t, J = 7.6 Hz, 1 H), 7.37 (br d, J = 8.9 Hz, 1 H), 7.47 (ddd, J = 8.9, 7.6, 1.2 Hz, 1 H), 7.96 (dd, J = 7.7, 1.4 Hz, 1 H), 8.07 (br d, J = 7.6 Hz, 1 H); IR (KBr) 1764 cm^{-1} (C=O); FABMS *m/e* 239 (M^+). Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.01; H, 5.45; N, 5.71.

Synthesis of Cannabifuran. To a solution of lithium diisopropylamide (47 mmol) in toluene (30 mL) at -78 °C were successively added ethyl heptanoate (7.33 g) and a toluene solution (40 mL) of 4-isopropyl-7-methyl-2-benzofuranaldehyde[3] (**9**, 6.06 g). The mixture was warmed to -10 °C and stirred for 2 h. The mixture was then hydrolyzed with a solution of AcOH (3.5 g) and water (50 mL), and was extracted with ether. The extract was dried ($MgSO_4$) and solvent was evaporated to give a β-hydroxyester as an orange oil: IR (neat) 3450 cm^{-1} (br, OH). A benzene solution

(150 mL) of the ester and *p*-toluenesulfonic acid (0.5 g) was boiled under reflux for 1 h to effect dehydration. Silica gel column chromatography (ether/hexane, 1:19) of the crude product afforded unsaturated ester **10** as a pale yellow oil (5.1 g): IR (neat) 1709 cm^{-1} (C=O), 1632 cm^{-1} (C=C). Compound **10** was stirred with diisobutylaluminium hydride (36 mmol) in toluene (50 mL) for 4 h at room temperature. The mixture was then treated with 1 N aq HCl (100 mL), and was extracted with ether. The extract was dried ($MgSO_4$). Evaporation of solvent gave allylic alcohol **11** (4.3 g). The alcohol was stirred with Ac_2O (2.0 g), NEt_3 (2.5 g), DMAP (4 mg), and ether (20 mL) for 2 h at room temperature. The mixture was then diluted with ether, and was washed (diluted aq HCl, saturated aq $NaHCO_3$, and water) and dried ($MgSO_4$). Evaporation of solvent gave crude acetate ester **12**. Purification by column chromatography on silica gel (ether/hexane, 1:19) gave pure (*E*)-3-(4-isopropyl-7-methyl-2-benzofuranyl)-2-pentylallyl acetate (**12**) as a colorless oil (3.88 g, 38% from **9**): ^1H NMR δ 0.91 (t, J = 7.2 Hz, 3 H), 1.33 (d, J = 7.0 Hz, 6 H), 1.26-1.46 (m, 4 H), 1.61 (m, 2 H), 2.13 (s, 3 H), 2.48 (s, 3 H), 2.61 (t, J = 8.1 Hz, 2 H), 3.18 (septet, J = 7.0, 1 H), 4.68 (d, J = 1.2 Hz, 2 H), 6.39 (s, 1 H), 6.68 (s, 1 H), 6.96 (d, J = 7.8 Hz, 1 H), 7.01 (d, J = 7.8 Hz, 1 H). Anal. Calcd for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 77.38; H, 8.77. The *E*-configuration of **12** was established by an NOE experiment. Irradiation of at δ 4.68 ($AcOCH_2$) increased the intensity of the signal at δ 6.39 (vinyl H) by 20%.

Ester **12** (1.027 g, 3 mmol) was cyclocarbonylated as described above. The reaction mixture was washed (diluted aq HCl, saturated aq $NaHCO_3$, and water) and dried ($MgSO_4$). Solvent was evaporated to give a brown oil, which was purified by column chromatography on silica gel (ether/hexane, 1:30) to give 1-acetoxy-9-isopropyl-

6-methyl-3-pentyldibenzofuran (**13**, 0.784 g, 74%) as a pale yellow oil: ^{1}H NMR δ 0.90 (t, *J* = 7.0 Hz, 3 H), 1.35 (d, *J* = 6.8 Hz, 6 H), 1.30–1.40 (m, 4 H), 1.70 (m, 2 H), 2.42 (s, 3 H), 2.53 (s, 3 H), 2.75 (t, *J* = 7.8 Hz, 2 H), 3.97 (septet, *J* = 6.8 Hz, 1 H), 6.89 (d, *J* = 1.2 Hz, 1 H), 7.15 (d, *J* = 7.6 Hz, 1 H), 7.22 (d, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 1.2 Hz, 1 H); IR (neat) 1778 cm^{-1} (C=O). Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.51; H, 7.85.

Acetate **13** (336 mg), KOH (440 mg), and MeOH (10 mL) were stirred for 1 h at room temperature. The mixture was acidified with 6 N aq HCl (5 mL), and was extracted with ether. The extract was dried ($MgSO_4$). Evaporation of solvent gave crude 9-isopropyl-6-methyl-3-pentyldibenzofuran-1-ol (**14**, 277 mg, 94%) as a pale yellow solid. Recrystallization (hexane) gave colorless prisms: mp 80–81 °C (lit.[3]) mp 78–79 °C, lit.[10]) mp 80–81 °C); ^{1}H NMR[2,3]) δ 0.89 (t, *J* = 7.0, 3 H), 1.28–1.30 (m, 4 H), 1.34 (d, *J* = 7.0, 6 H), 1.65 (m, 2 H), 2.53 (s, 3 H), 2.65 (t, *J* = 7.6 Hz, 2 H), 4.39 (septet, *J* = 7.0 Hz, 1 H), 5.23 (s, 1 H), 6.43 (s, 1 H), 7.01 (s, 1 H), 7.16 (d, *J* = 7.9 Hz, 1 H), 7.17 (d, *J* = 7.9 Hz, 1 H); IR (KBr) 3500 cm^{-1} (OH); ^{13}C NMR[16] δ 14.0, 15.0, 22.6, 24.3 (2C), 30.5, 31.0, 31.4, 35.8, 104.1, 109.8, 110.7, 118.4, 118.9, 121.3, 127.4, 142.0, 143.2, 149.7, 154.4, 158.3.

Acknowledgment. The author wishes to express his thanks to Professor Takamichi Yamagishi of Tokyo Metropolitan University for the recording of mass spectra.

References for Chapter 3

1) J. Tsuji, T. Yamakawa, M. Kaito, T. Mandai, *Tetrahedron Lett.*, 2075 (1978).

2) J. Friedrich-Friechtl, G. Spiteller, *Tetrahedron* **31**, 479 (1975).

3) M. V. Sargent and P. O. Stransky, *J. Chem. Soc., Perkin Trans. 1*, 1605 (1982).

4) Although the by-products were not identified, polymerization[5] of **15a** might have been caused by trace acidic impurities. Alternatively, thermal decomposition might have occurred. Attempted distillation, in vacuo, of **15a** at temperatures above 150 °C gave a dark blue viscous oil. Attempted purification of **15a** by silica gel column chromatography (ether/hexane, 2:1) at room temperature produced a similar color change, which also suggested decomposition.

5) L. Livingstone, in *Rodd'S Chemistry of Carbon Compounds*, 2nd ed., S. Coffey Ed.; Elsevier: Amsterdam, **1973**; Vol. 4, Part A, Chapter 4, pp 329, 335.

6) a) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *Chem. Lett.*, 377 (1988).

b) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *J. Org. Chem.* **53**, 3832 (1988).

c) M. Iwasaki, H. Matsuzaka, Y. Hiroe, Y. Ishii, and M. Hidai, *Chem. Lett.*, 1159 (1988).

7) a) K. H. Dötz in *Organometallics in Organic Synthesis*; A. de Meijere and H. tom Dieck, Eds.; Springer: Berlin, 1988; p 85.

b) W. D. Wulff in *Advances in Metal-Organic Chemistry*; L. S. Liebeskind, Ed.; JAI: Greenwich, CN, 1988; Vol. 1, p 209.

8) M. R. Kharasch, R. C. Seyler, and F. R. Mayo, *J. Am. Chem. Soc.*, **60**, 882 (1938).

9) K. Clarke, R. M. Scrowston, and M. T. Sutton, *J. Chem. Soc., Perkin Trans. 1*, 1196 (1973).

10) J. Novák, C. A. Salemink, *J. Chem. Soc., Perkin Trans. 1*, 2873 (1983).

Chapter 4

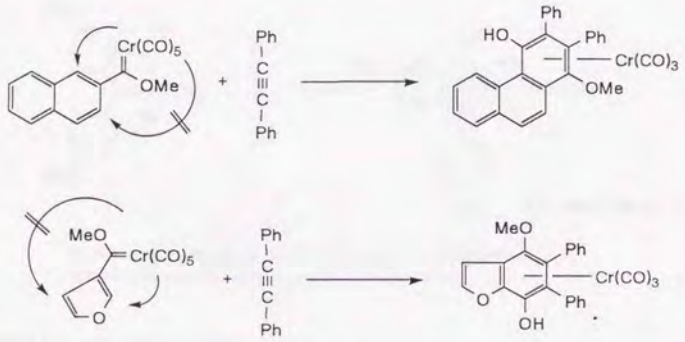
Palladium-Catalyzed Cyclocarbonylation of 3,3-Di(aryl)allyl Acetates

Abstract

Palladium-catalyzed cyclocarbonylation of 3,3-di(aryl)allyl acetates afforded *p*-(aryl)-substituted fused phenyl acetates where the cyclization occurred selectively on the more electron rich ring.

4-1. Introduction

In the course of the study on the palladium complex-catalyzed cyclocarbonylation of cinnamyl compounds, it was found that some selectivities of this reaction are very similar to those of benzannulation reaction of chromium-arylcarbene complexes with alkynes. When 3-(2-naphthyl)-, 3-(3-furyl)-, and 3-(3-thienyl)allyl acetates were cyclocarbonylated by a palladium catalyst, 4-phenanthryl acetate, 7-acetoxybenzofuran, and 7-acetoxybenzothiophene were selectively obtained, respectively, in good yields (Chapter 2, **Scheme 2.3** and Chapter 3, **Scheme 3.1**)[1], while it was reported that, when 2-naphthyl- and 3-furylcarbene-chromium complexes were allowed to react with tolan, phenanthrene and benzofuran skeletons were selectively formed, respectively (**Scheme 4.1**)[2].

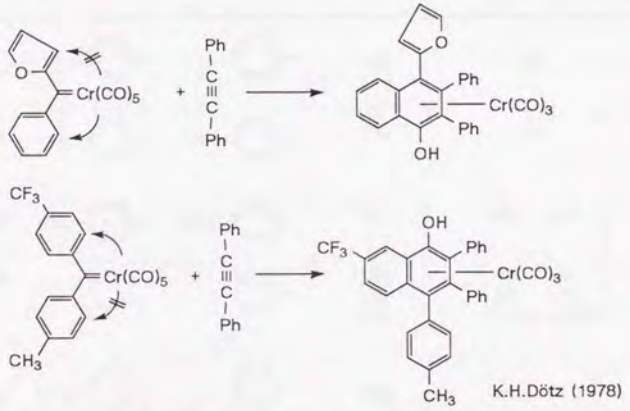


K.H.Dötz (1978)

Scheme 4.1
Benzannulation Reaction of Chromium-Arylcarbene Complexes with Tolan

These selectivities are in good accordance with those of electrophilic substitution of aromatic rings, and the similarities between the catalytic cyclocarbonylation and the benzannulation suggest that the cyclization step of these reactions proceeds through a

mechanism. Especially, the latter reaction has been considered to proceed via an alkenylketene chromium complex as an intermediate (see note).[2a] On the other hand, Dötz reported that the benzannulation of some diaryl-carbene chromium complexes having different aryl groups with tolan gave products formed by the cyclization at the more electron deficient aryl groups (**Scheme 4.2**)[2b]. In order to obtain information on the reaction mechanism of the catalytic cyclocarbonylation, the selectivity in the cyclo-carbonylation of 3,3-di(aryl)allyl acetates has been investigated.

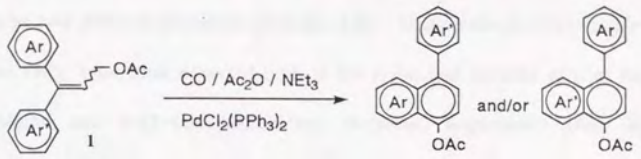


Scheme 4.2 Benzannulation Reaction of Unsymmetric Diarylcarbene-Chromium Complexes with Tolan.

4-2. Results and Discussion

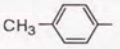
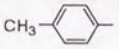
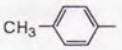
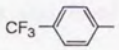
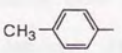
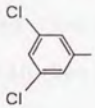
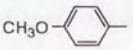
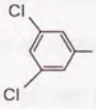
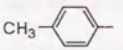
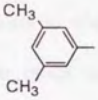
3,3-Diphenylallyl acetate (**1a**) was cyclocarbonylated to give 4-phenyl-1-naphthyl acetate (**2a**) in a good yield in the presence of CO, Ac_2O, NEt_3, and a catalytic amount of $PdCl_2(PPh_3)_2$ (**Table 4.1**, Run 1). The reaction was much slower than that of cinnamyl acetate, and the reaction time of 5-6 h was necessary to bring the reaction to completion even in the presence of 5% Pd-catalyst[3].

When an unsymmetrically disubstituted substrate was used, cyclization can *a priori*



Scheme 4.3 Palladium Catalyzed Cyclocarbonylationof γ,γ-Diarylallyl Acetates.

Table 4.1 Palladium Catalyzed Cyclocarbonylation of γ,γ-Diarylallyl Acetates*

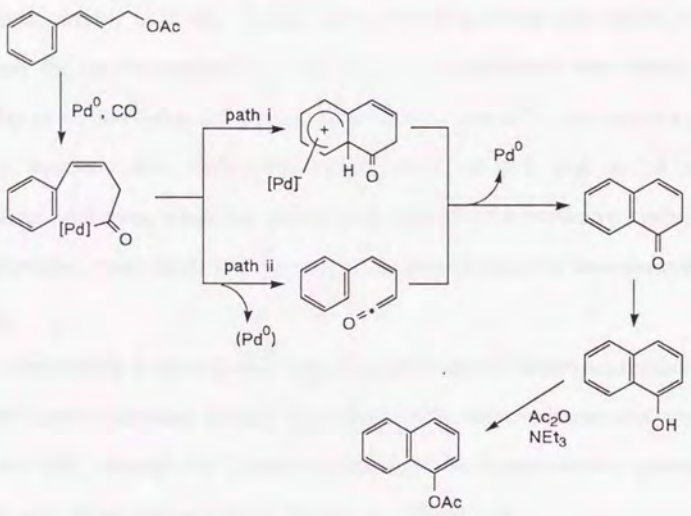
Run	Substrate	Ar	Ar'	Reaction Temp. / °C	Isolated Yield / % 2	3	
1	**1a**			160	72		
2	**1b**			160	84		
3	**1c**			160	56	33	**
4	**1d**			160	48	20	**
5				130	55	23	
6				100	trace	trace	
7	**1e**			160	41	0	
8	**1f**			160	29	5	
9	**1g**			160	39**	39**	

*Reaction conditions:
Substarte 5 mmol, $PdCl_2(PPh_3)_2$ 0.25 mmol, PPh_3 0.25 mmol, Ac_2O 10 mmol, NEt_3 11 mmol, benzene 5 mL, CO 55 kg/cm^2 at room temp., 160 °C, 6 h.

**Determined by GLC

occur at two different positions (**Scheme 4.3**). In the case of 3-(2-furyl)-3-phenylallyl acetate (**1d**), annulation occurred both at the furan and benzene ring to form 7-phenyl-benzofuran and 4-(2-furyl)naphthalene skeletons, respectively (Run 4), where the benzofuran derivative (**2d**) was predominantly formed, although the selectivity was not so remarkable probably because of high reaction temperature. It is clear that this selectivity did not arise from the *E*/*Z* isomer ratio of substrate because, with regard to **1d**, *E*-isomer (91 %) was contained much more than *Z*-isomer (9 %). If there was no *E*/*Z* isomerization under reaction conditions, the latter would have afforded **2d**, the major product in the actual reaction. The selectivity was not affected when the reaction was carried out at 130 °C (Run 5), but the reaction itself did not proceed at 100 °C (Run 6).

Similar selectivity was also found in the cyclocarbonylation of 3-(4-methyl-phenyl)-3-(4-trifluoromethylphenyl)allyl acetate (**1c**) (Run 3), where the two aryl substituents are expected to have the same steric effect on the annulation. The selectivity becomes more obvious when dichlorophenyl group was employed as the substituent of substrates (**1e** and **1f**) (Run 7, 8). Especially in the case of **1e**, although the starting material consisted of pure *Z*-isomer having acetoxymethyl moiety *cis*- to the dichlorophenyl group, the only product obtained from the reaction mixture was **2e** which was formed from the annulation on the tolyl group. The selectivities found for the reaction of **1e** and **1f** are considered to arise not from the steric hindrance by the chloro groups but from their electronic effect because the cyclocarbonylation of 3-(3,5-di-methylphenyl)-3-(4-methylphenyl)allyl acetate (**1g**) resulted in the formation of a 1:1 mixture of two isomeric products **2g** and **3g** (Run 9). These results clearly shows that cyclization occurred at the more electron rich rings.

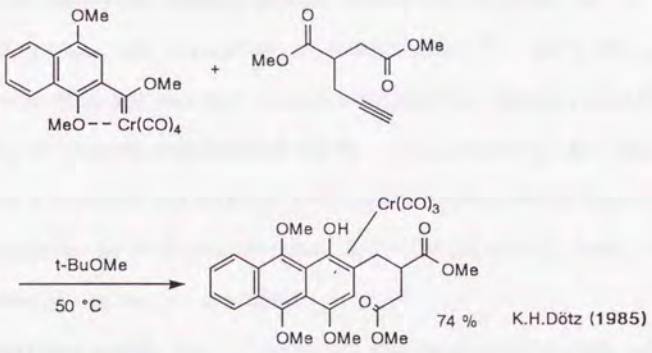


Scheme 4.4
Mechanism for Palladium Catalyzed Cyclocarbonylation.
[Pd] = $Pd(OAc)(PPh_3)_n$, n = 1, 2

We have already proposed[1a,b] a reaction mechanism for the cyclocarbonylation, which involves a intramolecular cyclization of intermediary acyl–palladium complexes such as $(Z\text{-}ArCH{=}CHCH_2CO)Pd(OAc)(PPh_3)_n$ or $(Z\text{-}ArCH_2CH{=}CHCO)Pd(OAc)(PPh_3)_n$ (n = 1,2), to afford cyclic ketones (**Scheme 4.4**). The subsequent isomerization to naphthol and acetylation produce the final product. At present two mechanisms are considered to be possible for the cyclization step. One involves the intramolecular electrophilic attack of the acyl group coordinated by palladium on the aromatic ring (path i) analogously to the Friedel–Crafts acylation. In the other mechanism, cyclization

proceeds via an alkenylketene intermediate formed by the β-elimination of the butenoyl-palladium complex (path ii). Participation of an alkenylketene intermediate was also proposed for the benzannulation reaction where the intermediate was formed by the coupling of a coordinating CO and the alkenylcarbene ligand.[2a] The selectivity shown here is consistent with electrophilic reaction on an aromatic ring, and is in good accordance with those which has already been found for the cyclocarbonylation.[1] On the other hand, these selectivities are opposite to those reported for benzannulation (*vide supra*).

Furthermore, it was reported[4] that a (1,4-dimethoxy-2-naphthylcarbene)chromium complex gives cyclization product in a good yield under benzannulation conditions (**Scheme 4.5**), although the cyclocarbonylation of 3-(1,4-dimethoxy-2-naphthyl)allyl acetate gave no cyclization product (Chapter 2, **Scheme 2.4**).



Scheme 4.5 Benzannulation reaction of (1,4-dimethoxy-2-naphthyl)carbenecomplex.

Considering these differences between both reactions, the mechanism including electrophilic attack of the acyl group (path i) seems to be more probable, although the

participation of the alkenylketene intermediate (path ii) cannot be completely denied because there is a large difference in reaction temperature between them, that is, 160 °C for the palladium catalyzed cyclocarbonylation and 50–70 °C for the benzannulation of arylcarbene complexes.

Conclusion

The cyclocarbonylation is shown to be effective for the synthesis of biaryl systems and its cyclization step is proved to be an electrophilic reaction by nature.

4–3. Experimental.

^1H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with a JEOL–GX400 spectrometer. Tetramethylsilane served as an internal standard. GLC analysis was performed with Shimadzu GC–14A instrument equipped with a flame ionization detector and a 25 m Hicap–CBP1 capillary column. Helium was the carrier gas.

$PdCl_2(PPh_3)_2$ was prepared by a published method.[5] Ac_2O, NEt_3, and all solvents were dried, and then were distilled under nitrogen. General procedure for the preparation of substrates was described for **1b**. The substrates **1c**, **d**, **f**, and **g** were obtained as *E/Z* mixtures and employed in the catalytic reaction without separation. The *E/Z* configurations of **1c–f** were determined by ^1H–^1H 2D–NOESY NMR. The *E/Z* configuration of **1g** was not determined.

3,3–Diphenylallyl acetate (1a). Colorless oil after purification by silica gel column chromatography (EtOAc/hexane, 1:19). Obtained in 73 % yield from benzophenone. ^1H NMR[6] δ 2.03 (s, 3H,–$COCH_3$), 4.63 (d, J = 7.0 Hz, 2H, CH_2), 6.18 (t, J = 7.0 Hz, 1H, vinyl), 7.15–7.34 (m, 10H, Ar). ^{13}C NMR δ 20.8, 62.5, 122.3, 127.5, 127.6, 127.7, 128.1, 128.2, 129.5, 138.6, 141.4, 146.2, 170.5.

3,3-Di(4-methylphenyl)allyl acetate (1b). A mixture of 4,4'-dimethylbenzophenone (50 mmol), ethyl bromoacetate (55 mmol), zinc (coarse powder, 55 mmol), $(MeO)_3B$ (20 mL), and THF (20 mL) was stirred for 16 h at room temperature. The mixture was then hydrolyzed with glycerin (20 mL) and aqueous NH_3 (28 %, 20 mL), and was extracted with ether. The extract was washed (H_2O) and dried ($MgSO_4$), and the solvent was evaporated to give a β-hydroxy ester (9.3 g, 63 %) as yellow blocks: IR (KBr) 1711 cm^{-1} (C=O), 3500 cm^{-1} (OH). A benzene solution (100 mL) of the ester (9.3 g) and *p*-toluenesulfonic acid (0.3 g) was boiled under reflux for 5 h to effect dehydration. The mixture was washed (10 % $NaHCO_3$, H_2O) and evaporation of the solvent gave a crude unsaturated ester as an yellow oil (9.0 g): IR (neat) 1726 cm^{-1} (C=O), 1610 cm^{-1} (C=C). The crude ester (9.0 g) was stirred with diisobutylaluminium hydride (75 mmol) in toluene (100 mL) for 16 h at room temperature. The mixture was then treated with 1 N aq HCl (100 mL) and was extracted with ether. Evaporation of the solvent and recrystallization from hexane gave allylic alcohol as colorless blocks (5.64 g). The alcohol (10 mmol) was stirred with Ac_2O (12 mmol), NEt_3 (15 mmol), DMAP (20 mg), and ether (20 mL) for 36 h at room temperature. The mixture was then diluted with ether, and was washed (diluted aq HCl, 10 % aq $NaHCO_3$, and water), and dried ($MgSO_4$). Evaporation of the solvent gave a white powder (2.6 g, 93 %). Recrystallization from hexane gave pure **1b** as colorless blocks. Mp 85–87 °C. ^1H NMR δ 2.06 (s, 3H, $COCH_3$), 2.32 (s, 3H, Ar-CH_3), 2.37 (s, 3H, Ar-CH_3), 4.63 (d, J = 7.0 Hz, 2H, CH_2), 6.11 (t, J = 7.0 Hz, 1H, vinyl), 7.04–7.21 (m, 8H, Ar). ^{13}C NMR δ 21.0, 21.1, 21.2, 62.8, 121.1, 127.6, 128.8, 128.9, 129.6, 135.8, 137.4, 137.6, 138.9, 146.2, 170.8.

3-(4-Methylphenyl)-3-(4-trifluoromethylphenyl)allyl acetate (1c, *E*/*Z* = 36:64). Pale

yellow solid after purification by silica gel column chromatography (EtOAc/hexane, 1:14). Obtained in 69 % yield from (4-methylphenyl)-(4-trifluoromethylphenyl)ketone. *E*-isomer; ^{1}H NMR δ 2.07 (s, 3H, $COCH_3$), 2.38 (s, 3H, Ar-CH_3), 4.67 (d, *J* = 6.9 Hz, 2H, CH_2), 6.20 (t, *J* = 6.9 Hz, 1H, vinyl), 7.05 (d, *J* = 7.9 Hz, 2H, Ar), 7.20 (d, *J* = 7.9 Hz, 2H, Ar), 7.36 (d, *J* = 7.9 Hz, 2H, Ar), 7.52 (d, *J* = 7.9 Hz, 2H, Ar). *Z*-isomer; ^{1}H NMR δ 2.06 (s, 3H, $COCH_3$), 2.33 (s, 3H, Ar-CH_3), 4.59 (d, *J* = 7.1 Hz, 2H, CH_2), 6.23 (t, *J* = 7.1 Hz, 1H, vinyl), 7.11 (s, 4H, Ar), 7.31 (d, *J* = 7.9 Hz, 2H, Ar), 7.64(d, *J* = 7.9 Hz, 2H, Ar).

3-(2-Furyl)-3-phenylallyl acetate (1d, *E*/*Z* = 91:9). Colorless oil after purification by silica gel column chromatography (EtOAc/hexane, 1:9). Obtained in 49 % yield from (2-furyl)phenylketone. *E*-isomer; ^{1}H NMR δ 2.03 (s, 3H, $COCH_3$), 4.58 (d, *J* = 7.3 Hz, 2H, CH_2), 5.91 (d, *J* = 3.4 Hz, 1H, furyl), 6.31 (dd, *J* = 1.8, 3.4 Hz, 1H, furyl), 6.37 (t, *J* = 7.3 Hz, 1H, vinyl), 7.24-7.28 and 7.33-7.48 (m, 6H, Ph and furyl). *Z*-isomer; ^{1}H NMR δ 2.09 (s, 3H, $COCH_3$), 5.10 (d, *J* = 6.1 Hz, 2H, CH_2), 5.78 (t, *J* = 6.1 Hz, 1H, vinyl), 6.24 (d, *J* = 3.4 Hz, 1H, furyl), 6.41 (dd, *J* = 1.8, 3.4 Hz, 1H, furyl), 7.24-7.28 and 7.33-7.48 (m, 6H, Ph and furyl).

(Z)-3-(2,5-Dichlorophenyl)-3-(4-methylphenyl)allyl acetate (1e). Colorless oil after purification by silica gel column chromatography (ether/hexane, 1:9). 39 % yield from (2,5-dichlorophenyl)(4-methylphenyl)ketone. ^{1}H NMR δ 2.08 (S, 3H, $COCH_3$), 2.34 (s, 3H, Ar-CH_3), 4.58 (d, *J* = 7.0 Hz, 2H, CH_2), 6.18 (t, *J* = 7.0 Hz, 1H, vinyl), 7.09 (d, *J* = 1.8 Hz, 2H, Ar), 7.10-7.11 (m, 4H, Ar), 7.35 (d, *J* = 1.8 Hz, 2H, Ar).

3-(2,5-Dichlorophenyl)-3-(4-methoxyphenyl)allyl acetate (1f, *E*/*Z* = 36:64). Colorless oil after purification by silica gel column chromatography (EtOAc/hexane, 1:7). Obtained in 78 % yield from (2,5-dichlorophenyl)(4-methoxyphenyl)ketone. Major isomer ^{1}H

NMR δ 2.08 (S, 3H, $COCH_3$), 3.81 (s, 3H, OCH_3), 4.56 (d, J = 7.0 Hz, 2H, CH_2), 6.14 (t, J = 7.0 Hz, 1H, vinyl), 6.84 (d, J = 9.2 Hz, 2H, Ar), 7.09 (d, J = 1.9 Hz, 2H, Ar), 7.14 (d, J = 9.2 Hz, 2H, Ar), 7.38 (t, J = 1.9 Hz, 1H, Ar). Minor isomer ^{1}H NMR δ 2.05 (s, 3H, $COCH_3$), 3.85 (s, 3H, OCH_3), 4.65 (d, J = 7.0 Hz, 2H, CH_2), 6.11 (t, J = 7.0 Hz, 1H, vinyl), 6.93 (d, J = 8.9 Hz, 2H, Ar), 7.07 (d, J = 8.9 Hz, 2H, Ar), 7.13 (d, J = 1.8 Hz, 2H, Ar), 7.26 (t, J = 1.8 Hz, 1H, Ar).

3-(2,5-Dimethylphenyl)-3-(4-methylphenyl)allyl acetate (1g, *E*/*Z* or *Z*/*E* = 53:47). Colorless oil after purification by silica gel column chromatography (EtOAc/hexane, 1:24). Obtained in 65 % yield from (2,5-dimethylphenyl)(4-methylphenyl)ketone. ^{1}H NMR δ 2.05 (s, 6H, $COCH_3$), 2.25 (s, 3H, *m*-CH_3), 2.29 (s, 3H, *m*-CH_3), 2.32 (s, 3H, *p'*-CH_3), 2.37 (s, 3H, *p'*-CH_3), 4.62 (d, J = 7.0 Hz, 2H, CH_2), 4.63 (d, J = 7.0 Hz, 2H, CH_2), 6.100 (t, J = 7.0 Hz, 1H, vinyl), 6.104 (t, J = 7.0 Hz, 1H, vinyl), 6.78 (s, 2H, *o*-H), 6.87 (s, 2H, *o*-H), 6.90 (s, 1H, *p*-H), 6.95 (s, 1H, *p*-H), 7.06 (d, J = 7.9 Hz, 2H, Ar), 7.07 (d, J = 7.9 Hz, 2H, Ar), 7.15 (d, J = 7.9 Hz, 2H, Ar), 7.17 (d, J = 7.9 Hz, 2H, Ar).

Palladium Catalyzed Cyclocarbonylation of 3,3-Diarylallyl Acetates. The following procedure is representative. A mixture of **1a** (5 mmol), $PdCl_2(PPh_3)_2$ (0.25 mmol), Ac_2O 10 mmol), NEt_3 (11 mmol), and benzene (4 mL) in a stainless steel autoclave was pressurized with CO (55 kg/cm^2 at room temperature) and was heated at 160 °C for 6 h with stirring. Then the autoclave was cooled and CO was discharged. The mixture was diluted with ether, washed (dilute aq HCl, saturated aq $NaHCO_3$, and water), and dried ($MgSO_4$). Solvent was evaporated and crude product was purified by silicagel column chromatography (EtOAc/Hexane, 1:19) and recrystallization (hexane) to give 4-phenyl-1-naphthyl acetate (**2a**) as pale orange blocks. Mp 69-70 °C. ^{1}H NMR

δ 2.41 (s, 3H, $COCH_3$), 7.29 (d, *J* = 7.6 Hz, 1H, Ar), 7.37 (d, *J* = 7.6 Hz, 1H, Ar), 7.39–7.52 (m, 6H, Ar), 7.80 (d, *J* = 8.4 Hz, 1H, Ar), 7.97 (d, *J* =8.4 Hz, 1H, Ar). ^{13}C NMR δ 21.0, 117.6, 121.3, 126.3, 126.4, 126.48, 126.50, 126.9, 127.4, 128.3, 130.1, 132.8, 138.5, 140.2, 146.1, 169.5.

7-Methyl-4-(4-methylphenyl)-1-naphthyl acetate (2b). Pale orange blocks from hexane. Mp 107–109 °C. ^1H NMR δ 2.44 (s, 3H, Ar-CH_3), 2.49 (s, 3H, $COCH_3$), 2.51 (s, 3H, Ar-CH_3), 7.23 (d, *J* = 7.6 Hz, 1H, Ar), 7.27 (d, *J* = 8.5 Hz, 1H, Ar), 7.28 (d, *J* = 8.0 Hz, 2H, Ar), 7.31 (d, *J* = 7.6 Hz, 1H, Ar), 7.36 (d, *J* = 8.0 Hz, 2H, Ar), 7.65 (s, 1H, Ar), 7.81 (d, *J* = 8.5 Hz, 1H, Ar). ^{13}C NMR δ 21.0, 21.2, 21.8, 117.7, 120.1, 125.4, 126.5, 127.1, 128.7, 128.9(2C), 130.0(2C), 131.2, 136.1, 136.9, 137.4, 138.3, 145.4, 169.7.

7-Methyl-4-(4-trifluoromethylphenyl)-1-naphthyl acetate (2c). Colorless needles from hexane. Mp 96–97 °C. ^1H NMR δ 2.50 (s, 3H, $COCH_3$), 2.52 (s, 3H, Ar-CH_3), 7.26 (d, *J* = 7.6 Hz, 1H, Ar), 7.30 (d, *J* = 8.5 Hz, 1H, Ar), 7.31 (d, *J* = 7.6 Hz, 1H, Ar), 7.57 (d, *J* = 7.9 Hz, 2H, Ar), 7.69 (s, 1H, Ar), 7.69 (d, *J* = 8.5 Hz, 1H, Ar), 7.73 (d, *J* = 7.9 Hz, 2H, Ar).

4-(4-Methylphenyl)-7-trifluoromethyl-1-naphthyl acetate (3c). Colorless needles from hexane. Mp 120–122 °C. ^1H NMR δ 2.45 (s, 3H, Ar-CH_3), 2.51 (s, 3H, $COCH_3$), 7.31 (d, *J* = 8.4 Hz, 2H, Ar), 7.33 (d, *J* = 8.4 Hz, 2H, Ar), 7.39 (d, *J* = 7.9 Hz, 1H, Ar), 7.52 (d, *J* = 7.9 Hz, 1H, Ar), 7.60 (d, *J* = 9.1 Hz, 1H, Ar), 8.03 (d, *J* = 9.1 Hz, 1H, Ar), 8.24 (s, 1H, Ar).

4-Acetoxy-7-phenylbenzofuran (2d). Pale brown blocks from benzene–hexane. Mp 52–54 °C. ^1H NMR δ 2.41 (s, 3H, $COCH_3$), 6.74 (d, *J* = 2.3 Hz, 1H, furyl), 7.09 (d, *J* = 7.09 Hz, 1H, Ar), 7.39 (t, *J* = 8.0 Hz, 1H, Ar), 7.44 (d, *J* = 7.9 Hz, 1H, Ar),

7.49 (t, J = 8.0 Hz, 2H, Ar), 7.66 (d, J = 2.3 Hz, 1H, furyl), 7.81 (d, J = 8.0 Hz, 2H, Ar). ^{13}C NMR δ 21.0, 104.0, 115.8, 121.6, 123.8, 124.1, 127.7, 128.58, 128.61, 135.9, 143.0, 145.1, 153.2, 169.0.

4-(2-Furyl)-1-naphthyl acetate (3d). Pale brown blocks from benzene–hexane. Mp 86–89 °C. ^{1}H NMR δ 2.48 (s, 3H, $COCH_3$), 6.58 (dd, J = 1.8, 3.4 Hz, 1H, furyl), 6.69 (dd, J = 0.6, 3.4 Hz, 1H, furyl), 7.29 (d, J = 7.9 Hz, Ar), 7.53–7.58 (m, 2H, Ar), 7.62 (dd, J = 0.6, 1.8 Hz, 1H, furyl), 7.70 (d, J = 7.9 Hz, 1H, Ar), 7.92–7.94 (m, 1H, Ar), 8.39–8.41 (m, 1H, Ar). ^{13}C NMR δ 21.0, 109.4, 111.4, 117.7, 121.5, 125.9, 126.0, 126.5, 127.00, 127.04, 127.1, 131.7, 142.5, 146.6, 152.9, 169.3.

4-(2,5-Dichlorophenyl)-7-methyl-1-naphthyl acetate (2e). Colorless needles from hexane. Mp 159–161 °C. ^{1}H NMR δ 2.51 (s, 3H, $COCH_3$), 2.54 (s, 3H, Ar–CH_3), 7.25 (d, J = 7.5 Hz, 1H, Ar), 7.30 (d, J = 7.5 Hz, 1H, Ar), 7.33 (d, J = 8.6 Hz, 1H, Ar), 7.36 (d, J = 2.1 Hz, 2H, Ar), 7.43 (t, J = 2.1 Hz, 1H, Ar), 7.68 (s, 1H, Ar), 7.70 (d, J = 8.6 Hz, 1H, Ar). ^{13}C NMR δ 21.1, 21.9, 117.7, 120.5, 125.62, 125.64, 127.2, 127.5, 128.5, 129.4, 130.6, 134.8, 135.4, 136.6, 143.4, 16.4, 169.5.

4-(2,5-Dichlorophenyl)-7-methoxy-1-naphthyl acetate (2f). Pale yellow needles from hexane. Mp 163–165 °C. ^{1}H NMR δ 2.49 (s, 3H, $COCH_3$), 3.92 (s, 3H, OCH_3), 7.14–7.17 (m, 2H, Ar), 7.20 (d, J = 7.8 Hz, 1H, Ar), 7.25 (d, J = 7.8 Hz, 1H, Ar); 7.34 (d, J = 1.8 Hz, 2H, Ar), 7.41 (t, J = 1.8 Hz, 1H, Ar), 7.70 (d, J = 8.9 Hz, 1H, Ar). ^{13}C NMR δ 21.1, 55.3, 100.0, 118.2, 119.5, 124.2, 127.46, 127.49, 127.8, 128.3, 128.5, 134.8, 135.4, 143.3, 145.8, 158.2, 169.3.

6,8-Dichloro-4-(4-methoxyphenyl)-1-naphthyl acetate (3f). Pale yellow needles from hexane. Mp 131–135 °C. ^{1}H NMR δ 2.44 (s, 3H, $COCH_3$), 3.89 (s, 3H, OCH_3), 7.03 (d, J = 8.4 Hz, 2H, Ar), 7.21(d, J = 7.8 Hz, 1H, Ar), 7.31 (d, J = 8.4 Hz, 2H, Ar),

7.43 (d, J = 7.8 Hz, 1H, Ar), 7.55 (d, J = 2.1 Hz, 1H, Ar), 7.79 (d, J = 2.1 Hz, 1H, Ar). ^{13}C NMR δ 21.7, 55.4, 114.1, 121.3, 125.3, 128.6, 129.4, 129.9, 130.6, 131.1, 131.3, 131.8, 135.7, 138.7, 145.1, 159.4, 170.2.

4-(2,5-Dimethylphenyl)-7-methyl-1-naphthyl acetate (2g). Obtained as a colorless oil which was a mixture with **3g**. ^{1}H NMR δ 2.39 (s, 6H, m-CH_3), 2.49 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 7.06-7.08 (m, 3H, Ar), 7.21-7.33 (m, 3H, Ar), 7.65 (s, 1H, Ar), 7.81 (d, J = 8.5 Hz, 1H, Ar).

6,8-Dimethyl-4-(4-methylphenyl)-1-naphthyl acetate (3g). Recrystallization of a mixture with **2g** from hexane gave pure **3g** as colorless blocks. Mp 118-120 °C. ^{1}H NMR δ 2.34 (s, 3H, Ar-CH_3), 2.42 (s, 3H, $COCH_3$), 2.45 (s, 3H, Ar-CH_3), 2.78 (s, 3H, Ar-CH_3), 7.07 (d, J = 7.9 Hz, 1H, Ar), 7.11 (br s, 1H, Ar), 7.27-7.34 (m, 5H, Ar), 7.49 (br s, 1H, Ar). ^{13}C NMR δ 21.2, 21.5, 21.7, 23.8, 118.5, 124.2, 124.8, 126.5, 128.9, 130.0, 131.8, 132.3, 134.7, 135.4, 136.8, 138.2, 138.6, 146.8, 170.1.

References for Chapter 4

1 a) M. Iwasaki, J.-P. Li, Y. Kobayashi, H. Matsuzaka, Y. Ishii, and M. Hidai, *J. Org. Chem.*, in press.

b) H. Matsuzaka, Y. Hiroe, M. Iwasaki, Y. Ishii, Y. Koyasu, and M. Hidai, *J. Org. Chem.*, **53**, 3832 (1988).

c) M. Iwasaki, J.-P. Li, Y. Kobayashi, H. Matsuzaka, Y. Ishii, and M. Hidai, *Tetrahedron Lett*, **30**, 95 (1989).

d) M. Iwasaki, H. Matsuzaka, Y. Hiroe, Y. Ishii, Y. Koyasu, and M. Hidai, *Chem. Lett.*, 1159 (1989).

2 a) K. H. Dötz, *Angew. Chem., Int. Ed. Engl.*, **23**, 587 (1984).

b) K. H. Dötz and R. Dietz, *Chem. Ber.*, **111**, 2517 (1978).

3 Cinnamyl acetate was cyclocarbonylated to 1-naphthyl acetate under similar conditions as indicated for **Table 4.1** in 81 % yield (Reaction time 1.5 h. See ref. 1c) or Chapter 3, **Table 3.3**, Run 5). Judging from the CO absorption, this reaction was completed within 0.5 h.

4 K. H. Dötz and M. Popall, *Tetrahedron*, **41**, 5797 (1985).

5 M. R. Kharasch, R. C. Seyler, and F. R. Mayo, *J. Am. Chem. Soc.*, **60**, 882 (1938).

6 a) T. Morimoto, M. Hirano, and T. Koyama, *J.Chem. Soc.,Perkin Trans.* 2, 1109 (1985).

b) K. Kurosawa and T. Tsujita, *Bull. Chem. Soc. Jpn.*, **54**, 2391 (1981).

7 K. H. Dötz and B. Fügen-Köster, *Chem. Ber.*, **113**, 1449 (1980).

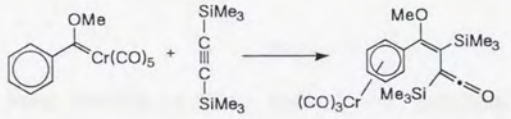
8 B. J. Anderson and W. D. Wulff, *J. Am. Chem. Soc.*, **112**, 8615 (1990).

9 K. H. Dötz and R. Dietz, *J. Organomet. Chem.*, **157**, C55 (1978).

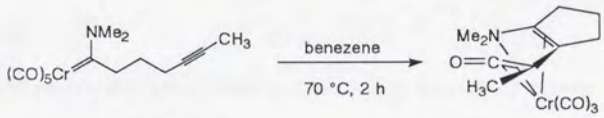
Notes

On the mechanism of the benzannulation, the following results are reported as the evidences which suggest the existence of alkenylketene intermediates.

1) Formation of alkenylketene complexes from carbene complexes and alkynes.



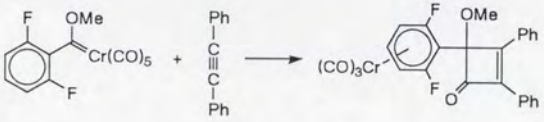
K.H.Dötz (1980).[7]

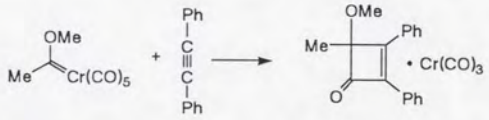


43 %

W.D.Wulff (1990).[8]

2) Isolation of cyclobutenones possibly formed by cyclization of alkenylketene moieties.





K.H.Dötz (1978).[9]

Chapter 5

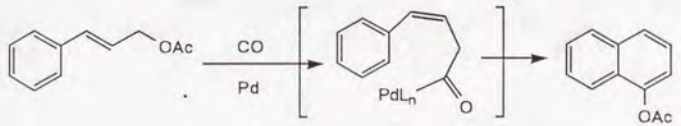
Novel Synthesis of Phenol Derivatives by Palladium-Catalyzed Cyclocarbonylation of 2,4-Pentadienyl Acetates

Abstract

Palladium-catalyzed cyclocarbonylation of 2,4-pentadienyl acetates in the presence of NEt_3 and AC_2O selectively gives phenyl acetates in good yields. This reaction provides a versatile and general synthetic route for the synthesis of substituted phenols including 3,5- or 2,3-disubstituted phenyl esters, which are hardly obtainable by conventional electrophilic substitution reactions of phenol.

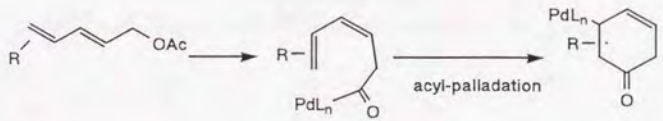
5-1. Introduction

As described in the preceding chapters, the palladium catalyzed cyclocarbonylation is considered to proceed via an acyl-palladium complex (**1**) derived from allylic compound, CO, and palladium(0) complex (**Scheme 5.1**). It is expected that a suitable choice of substrates would make it possible for such an acyl complex to react with an organic moiety other than aromatic rings. Among such reactions, the carbonylation of an allyl compound having another C=C double bond within a molecule seems attractive because the double bond would insert into the acyl-palladium bond (**Scheme 5.2**). The insertion of a carbon-carbon multiple bond into an acyl-metal bond is known as "acyl-metalation", (Chapter 1, **1-3-1**). Typical examples of them are illustrated in **Scheme 5.3**,[1] and **5.4**.[2] The reactions illustrated in **Scheme 5.4** are discussed later in this chapter. Although so many are reported on acyl-metalation, their application for the syntheses of six-membered aromatic rings are very few. One example is the nickel catalyzed synthesis of *m*-cresol from methallyl chloride, acetylene, and CO (**Scheme 5.5**).[3] It was proposed that this reaction involved an intramolecular acyl-nickelation of



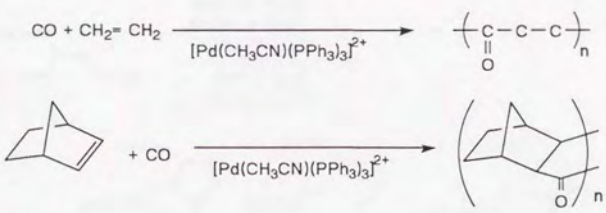
1

Scheme 5.1 Cinnamyl System.



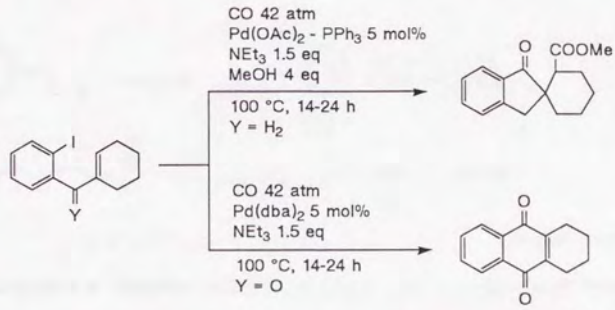
1'

Scheme 5.2 2,4-Pentadienyl System.



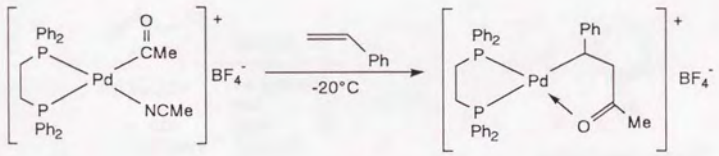
(a)

A.Sen (1982)[1a)]



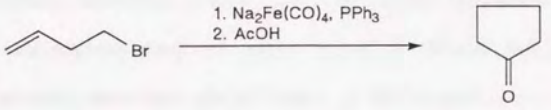
(b)

E.Negishi (1986)[1b)]



(c)

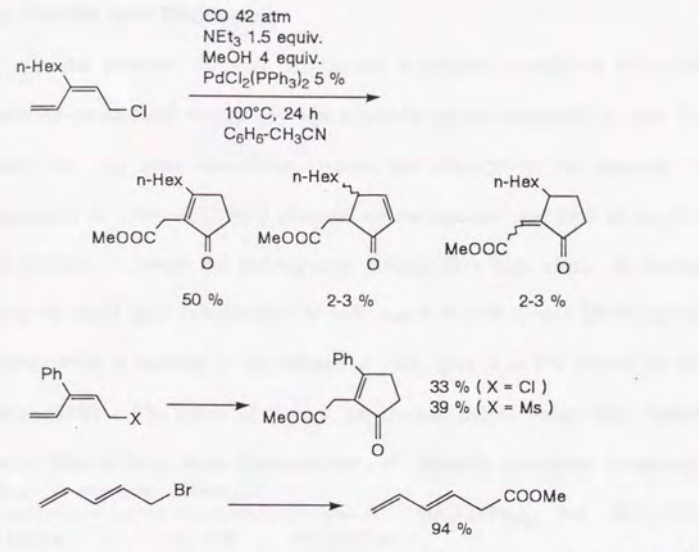
F.Ozawa and A.Yamamoto (1990)[1c)]



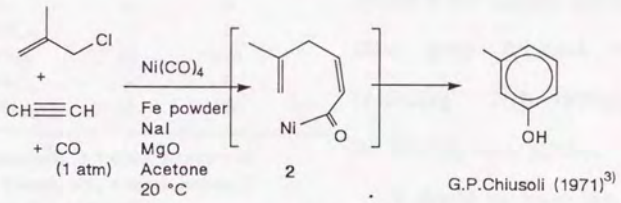
(d)

J.P.Collman (1975)[1d,e)]

Scheme 5.3 Acyl-Metalation Reactions.



Scheme 5.4 Palladium Catalyzed Carbonylation of *Z*-2,4-Pentadienyl Compounds.



Scheme 5.5 Ni-Catalyzed Formation of *m*-cresol from Metallyl Chloride , Acetylene, and CO.

an intermediary acyl-nickel complex (**2**). As another application of the palladium-catalyzed cyclocarbonylation, the author wishes to describe that of 2,4-pentadienyl acetates affording substituted phenyl acetates in this chapter.

5-2. Results and Discussion.

In the presence of NEt_3, Ac_2O, and a catalytic amount of $PdCl_2(PPh_3)_2$, 5-phenyl-2,4-pentadienyl acetate (**3**) was smoothly cyclocarbonylated to give 2-acetoxybiphenyl **4**. No other identifiable product was detected by GC analysis. Reaction temperatures of 120-140°C were adequate for the reaction, and both of Ac_2O and NEt_3 were essential to obtain the carbonylation product in a high yield. A reaction in the absence of Ac_2O gave 2-biphenylol in 16% and **4** in 11% (conv. 100%) as identifiable products, while a reaction in the absence of NEt_3 gave **4** in 9% (based on the starting **3**, conv. 52%). The effect of catalyst are summarized in **Table 5.1**. Palladium and platinum phosphine complexes such as $PdCl_2(PPh_3)_2$ and $PtCl_2(PPh_3)_2$ are effective catalysts, and some ruthenium complexes such as $RuCl_2(PPh_3)_3$ showed a low catalytic activity (run 8). Other group 8 metal compounds including $NiBr_2(PPh_3)_2$ and $RhCl(PPh_3)_3$ were inactive.

Table 5.1 Effect of Catalyst on the Cyclocarbonylation of 5-Phenyl-2,4-pentadienyl Acetate (**3**)[a].

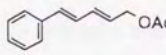
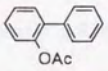
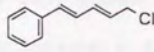
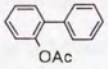
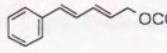
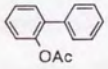
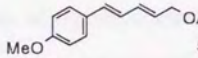
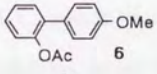
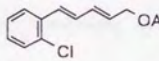
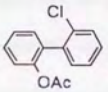
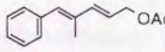
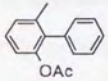
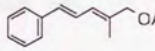
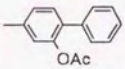
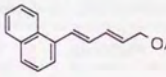
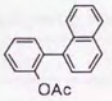
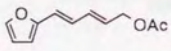
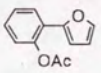
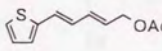
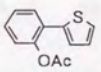
Run	Catalyst	Conv. / %	Yield of **4**[b] / %
1	$PdCl_2(PPh_3)_2$	100	74
2	$PdCl_2(PMe_2Ph)_2$	100	75
3	$Pd(PPh_3)_4$	100	76
4	$Pd(OAc)_2$	-	0
5	$NiBr_2(PPh_3)_2$	-	0
6	$PtCl_2(PPh_3)_2$	91	76
7	$RhCl(PPh_3)_3$	-	0
8	$RuCl_2(PPh_3)_3$	44	26

a) Reaction conditions: **3** 3 mmol, catalyst 0.09 mmol, Ac_2O 6 mmol, NEt_3 6 mmol, benzene 5 mL, CO 50 atm (at r.t.), 140 °C, 3h.
b) Determined by GLC

It should be noted that acetate **3** was converted to **4** in a much higher yield than the corresponding chloride (33%, **Table 5.2**, Run 2) or ethyl carbonate (29%, Run 3), although allylic acetates have been claimed to be poor substrates for carbonylation reactions.[4)]

As shown in **Table 5.2** and **5.3**, various substituted phenyl esters were obtained in moderate to high yields by this unique cyclocarbonylation. Especially, 5-aryl-2,4-

Table 5.2 Cyclocarbonylation of Substituted 5-Aryl-2,4-pentadienyl Acetates[a]

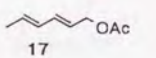
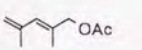
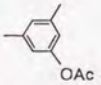
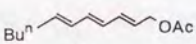
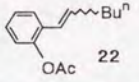
Run	Substrate	Product	Isolated Yield (%)[b]
1	 3	 4	69 (74)
2	 3'	 4	(33)
3	 3"	 4	(24)
4	 5	 6	73
5	 7	 8	84
6	 9	 10	57
7	 11	 12	46
8	 13	 14	79
9	 15	 16	57
10			53

[a] Reaction conditions:
substrate 3 mmol, $PdCl_2(PPh_3)_2$ 0.09 mmol, Ac_2O 6 mmol,
NEt_3 6.6 mmol, benzene 5 ml, CO 50 atm, 140 °C, 3h.

[b] GC yield in parentheses.

pentadienyl acetates are good substrates for this reaction and substituents at 2- or 4-position of the substrates seem to lower the yields of the products. In the reaction of *trans,trans,trans*-2,4,6-undecatrienyl acetate, the six-membered ring formation again exclusively occurred to give *o*-(1-hexenyl)phenyl acetate, but the product was a mixture of the *cis* and *trans* isomers (**Table 5.3**, run 3). It is noteworthy that the present carbonylation is applicable to the synthesis of 3,5- and 2,3-disubstituted phenyl acetates (**Table 5.2**, run 6 and **Table 5.3**, run 2, respectively), which are difficult to be prepared by conventional electrophilic substitution reactions of phenol. This exemplifies the effectiveness of the cyclocarbonylation as a synthetic method for substituted phenols. However, when *E*-3,5-di(*p*-tolyl)-2,4-pentadienyl acetate (**23**) was carbonylated under similar reaction conditions, cyclization toward the tolyl group at 3-position competed with the phenyl acetate formation to give naphthyl acetate **24** (17%) concurrent with the expected 2,4-di(*p*-tolyl)phenyl acetate (38%) in spite of the *E* configuration of the substrate (**Scheme 5.6**).

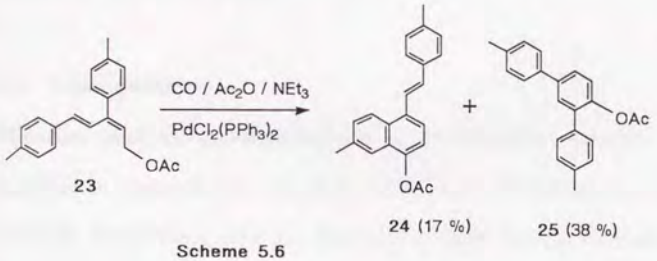
Table 5.3 Cyclocarbonylation of Substituted 2,4-Pentadienyl Acetates*

Run	Substrate	Product	Isolated Yield (%)
1	 **17**	 **18**	51
2	 **19**	 **20**	40
3	 **21**	 **22**	52**

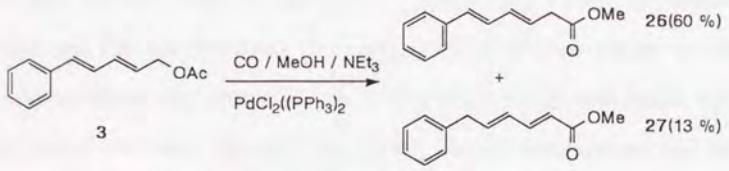
*Reaction conditions: substrate 3 mmol, $PdCl_2(PPh_3)_2$ 0.09 mmol, Ac_2O 6 mmol, NEt_3 6.6 mmol, benzene 5 ml, CO 50 atm, 140 °C, 3h.
**trans / cis = 79 / 21.

Previously, Negishi reported that palladium-catalyzed cyclocarbonylation of *cis*-2,4-pentadienyl chlorides in the presence of MeOH and NEt_3 yields cyclopentenone derivatives, and that the *cis* configuration of the substrates is required for the cyclization (**Scheme 5.4**).[2] Although the catalytic systems are closely related to each other, the cyclocarbonylation described here is in sharp contrast to Negishi's reaction in that only six-membered products, but not five-membered ones, are selectively obtained and that substrates of *trans* configuration smoothly undergo the cyclization. The latter point is especially advantageous from a synthetic point of view. As expected, carbonylation of **3** under Negishi's conditions resulted in the formation of methyl (3*E*,5*E*)-6-phenyl-3,5-hexadienoate (60%) and methyl (2*E*,4*E*)-6-phenyl-2,4-hexadienoate (13%, **Scheme 5.7**).

The present reaction is considered to proceed via a hexadienoylpalladium complex **1** (**Scheme 5.2**) , which is generated by oxidative addition of a pentadienyl acetate to



Scheme 5.6



Scheme 5.7

a Pd(0) species followed by CO insertion. In the absence of a nucleophile such as MeOH, the hexadienoylpalladium complex would undergo *cis–trans* isomerization of the internal double bond and intramolecular insertion of the terminal C=C double bond into the Pd–C bond. Subsequent β–elimination gives a cyclohexadienone, which tautomerizes to afford the corresponding phenol and is finally acetylated by Ac_2O. Further investigation is necessary to elucidate the reason why the hexadienoyl palladium species selectively cyclizes to form a six–membered ring but not a five–membered one under the present reaction conditions.

Conclusion

The palladium cyclocarbonylation of 2,4–pentadienyl acetates was found to be effective for the general preparation of substituted phenols including 3,5– or 2,3–di–substituted phenyl esters which were hardly obtainable by conventional electrophilic substitution reaction of phenol.

5–3. Experimental.

Palladium catalyzed cyclocarbonylation of 2,4–pentadienyl acetates. The following procedure is representative. A mixture of 5–phenyl–2,4–pentadienyl acetate (0.606 g, 3 mmol), $PdCl_2(PPh_3)_2$ (63.2 mg, 0.09 mmol), Ac_2O (0.613g, 6 mmol), NEt_3 (0.668g, 6.6 mmol), and benzene (10 mL) in a stainless steel autoclave was pressurized with CO (50 atm) and was heated at 140°C for 3 h with stirring. Then the autoclave was cooled and CO was discharged. GLC analysis of the reaction mixture revealed that 2–acetoxybiphenyl was formed in 71%. The reaction mixture was diluted with ether, was washed with water, and dried over $MgSO_4$. Solvent was evaporated and the crude product was purified by silica gel column chromatography (hexane/ether, 6:1) and

bulb-to-bulb distillation to give pure 2-acetoxybiphenyl (69%) as colorless crystals.

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent and with $SiMe_4$ as an internal standard.

5-Phenyl-2,4-pentadienyl acetate (3). Colorless crystals: mp 60-62 °C; ^1H NMR δ 2.09 (3 H, s), 4.65 (2 H, d, *J* = 6.6 Hz), 5.87 (1 H, dt, *J* = 15.2, 6.6 Hz), 6.45 (1H, dd, 15.2, 10.5 Hz), 6.59 (1 H, d, 15.5 Hz), 6.77 (1 H, dd, 15.5, 10.5 Hz); ^{13}C NMR δ 170.7, 136.9, 134.5, 133.8, 128.6, 127.8, 127.7, 126.9, 126.5, 64.7, 20.9; IR (KBr) 1740 cm^{-1} (C=O); HREIMS calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.1011.

(1*E*,3*E*)-5-Chloro-1-phenyl-1,3-pentadiene (3'). Pale yellow crystals: mp 43-48 °C (lit.[5] mp 50-51 °C); ^1H NMR δ 4.18 (2 H, d, *J* = 7.3 Hz), 5.92 (1 H, dt, *J* = 15.0, 7.3 Hz), 6.46 (1 H, dd, *J* = 15.0, 10.1 Hz), 6.60 (1 H, d, *J* = 15.5 Hz), 6.77 (1 H, dd, *J* = 15.5, 10.1 Hz), 7.22-7.45 (5 H, m); ^{13}C NMR δ 45.2, 126.6, 127.3, 128.0, 128.5, 128.7, 134.3, 134.6, 136.8; HREIMS calcd for $C_{11}H_{11}Cl$ 178.0550, found 178.0565.

Ethyl (2*E*,4*E*)-5-phenyl-2,4-pentadienyl carbonate (3"). Colorless oil: ^1H NMR δ 1.32 (3 H, t, *J* = 7.2 Hz), 4.22 (2 H, q, *J* = 7.2 Hz), 4.71 (2 H, d, *J* = 6.7 Hz), 5.89 (1 H, dt, *J* = 14.9, 6.7 Hz), 6.49 (1 H, dd, *J* = 14.9, 10.5 Hz), 6.60 (1 H, d, *J* = 15.6 Hz), 6.77 (1 H, dd, *J* = 15.6, 10.5 Hz), 7.22-7.41 (5 H, m); ^{13}C NMR δ 14.3, 64.0, 67.9, 126.2, 126.5, 127.6, 127.9, 128.6, 134.1, 135.0, 136.8, 155.0; IR (neat) 1745 cm^{-1} (C=O).

(2*E*,4*E*)-(4-Methoxyphenyl)-2,4-pentadienyl acetate (5). Colorless crystals: mp 63-64 °C; ^1H NMR δ 2.08 (3 H, s), 3.81 (3 H, s), 6.64 (2 H, d, *J* = 6.7 Hz), 6.82 (1 H, dt, *J* = 15.1, 6.7 Hz), 6.43 (1 H, dd, *J* = 15.1, 10.3 Hz), 6.54 (1 H, d, *J* = 15.6 Hz), 6.65 (1 H, dd, *J* = 15.6, 10.3 Hz), 6.86 (2 H, d, *J* = 8.7 Hz), 7.33 (2 H, d, *J* = 8.7

Hz); ^{13}C NMR δ 21.0, 55.3, 64.9, 114.1, 125.66, 125.70, 127.7, 129.8, 133.4, 135.0, 159.5, 170.8; IR (KBr) 1740 cm^{-1} (C=O).

(2*E*,4*E*)-5-(2-Chlorophenyl)-2,4-pentadienyl acetate (7). Colorless oil: ^1H NMR δ 2.10 (3 H, s), 4.67 (2 H, d, *J* = 6.4 Hz), 5.93 (1 H, dt, *J* = 15.3, 6.4 Hz), 6.52 (1 H, dd, *J* = 15.3, 10.7 Hz), 6.75 (1 H, dd, *J* = 15.6, 10.7 Hz), 6.99 (1 H, d, *J* = 15.6 Hz), 7.17 (1 H, td, *J* = 7.6, 1.5 Hz), 7.23 (1 H, td, *J* = 7.6, 1.5 Hz), 7.36 (1H, dd, *J* = 7.6, 1.5 Hz), 7.56 (1H, dd, *J* = 7.6, 1.5 Hz); ^{13}C NMR δ 20.9, 64.5, 126.3, 126.8, 128.1, 128.7, 129.4, 129.8, 130.1, 132.3, 134.1, 134.9, 170.7; IR (neat) 1740 cm^{-1} (C=O); HREIMS calcd for $C_{13}H_{13}O_2Cl$ 236.0605, found 236.0581.

(2*E*,4*E*)-4-Methyl-5-phenyl-2,4-pentadienyl acetate (9). Colorless oil: ^1H NMR δ 2.00 (3 H, d, *J* = 1.2 Hz), 2.10 (3 H, s), 4.69 (2 H, d, *J* = 6.7 Hz), 5.85 (1 H, dt, *J* = 15.3, 6.7 Hz), 6.49 (1 H, d, *J* = 15.3 Hz), 6.56 (1 H, br s), 7.21–7.36 (5 H, m); ^{13}C NMR δ 13.8, 21.0, 65.2, 122.3, 126.8, 128.2, 129.2, 132.7, 134.7, 137.5, 139.6, 170.9; IR (neat) 1745 cm^{-1} (C=O); HREIMS calcd for $C_{14}H_{16}O_2$ 216.1151, found 216.1161.

(2*E*,4*E*)-2-Methyl-5-phenyl-2,4-pentadienyl acetate (11). Colorless crystals: mp 35–36 °C; ^1H NMR δ 1.89 (3 H, s), 2.10 (3 H, s), 4.58 (2 H, s), 6.24 (1 H, d, *J* = 11.0 Hz), 6.58 (1 H, d, *J* = 15.6 Hz), 6.99 (1 H, dd, *J* = 15.6, 11.0 Hz), 7.22 (1 H, t, *J* = 7.3 Hz), 7.32 (2 H, t, *J* = 7.3 Hz), 7.42 (2 H, d, *J* = 7.3 Hz); ^{13}C NMR δ 14.7, 21.0, 69.7, 124.2, 126.4, 127.6, 128.3, 128.6, 132.7, 133.3, 137.4, 170.9; IR (KBr) 1737 cm^{-1} (C=O); HREIMS calcd for $C_{14}H_{16}O_2$ 216.1151, found 216.1150.

(2*E*,4*E*)-5-(1-Naphthyl)-2,4-pentadienyl acetate (13). Colorless crystals: mp 45–47 °C; ^1H NMR δ 2.11 (3 H, s), 4.70 (2 H, d, *J* = 6.6 Hz), 5.94 (1 H, dt, *J* = 15.3, 6.6 Hz), 6.61 (1 H, dd, *J* = 15.3, 10.7 Hz), 6.83 (1 H, dd, *J* = 15.3, 10.7 Hz), 7.37 (1 H,

d, J = 15.3 Hz), 7.45 (1 H, t, J = 7.8 Hz), 7.47–7.54 (2 H, m), 7.65 (1 H, d, J = 7.8 Hz), 7.78 (1 H, d, J = 7.8 Hz), 7.85 (1 H, d, J = 7.3 Hz), 8.12 (1 H, d, J = 7.9 Hz); ^{13}C NMR δ 21.0, 64.7, 123.47, 123.51, 125.6, 125.8, 126.1, 127.2, 128.2, 128.6, 130.5, 131.1, 133.7, 134.3, 134.7, 170.7; IR (KBr) 1735 cm^{-1} (C=O).

(2*E*,4*E*)-5-(2-Furyl)-2,4-pentadienyl acetate (15). Colorless oil: ^{1}H NMR δ 2.02 (3 H, s), 4.57 (2 H, d, J = 6.4 Hz), 5.79 (1 H, dt, J = 15.4, 6.4 Hz), 6.22 (1 H, d, J = 3.4 Hz), 6.28–6.34 (3 H, m), 6.61 (1 H, dd, J = 15.6, 11.0 Hz), 7.30 (1 H, d, J = 1.5 Hz); ^{13}C NMR δ 20.9, 64.7, 109.0, 111.6, 121.2, 126.3, 127.0, 134.1, 142.4, 152.8, 170.7; IR (neat) 1737 cm^{-1} (C=O).

(2*E*,4*E*)-2,4-Hexadienyl acetate (17). Colorless oil: ^{1}H NMR δ 1.77 (3 H, d, J = 6.7 Hz), 2.06 (3 H, s), 4.57 (2 H, d, J = 6.7 Hz), 5.63 (1 H, dt, J = 15.3, 6.7 Hz), 5.76 (1 H, dq, J = 15.0, 6.7 Hz), 6.05 (1 H, dd, J = 15.0, 10.7 Hz), 6.25 (1 H, dd, 15.3, 10.7 Hz); ^{13}C NMR 18.1, 21.0, 65.0, 123.7, 130.5, 131.3, 134.9, 170.8; IR (neat) 1738 cm^{-1} (C=O); HREIMS calcd for $C_8H_{12}O_2$ 140.0838, found 140.0837.

(*E*)-Dimethyl-2,4-pentadienyl acetate (19). Colorless oil: ^{1}H NMR δ 1.84 (3 H, s), 1.87 (3 H, s), 2.10 (3 H, s), 4.50 (2 H, s), 4.87 (1 H, s), 5.03 (1 H, s), 5.92 (1 H, s); ^{13}C NMR δ 15.5, 21.0, 23.3, 70.4, 115.9, 130.3, 131.4, 141.1, 170.9; IR (neat) 1745 cm^{-1} (C=O); HREIMS calcd for $C_9H_{14}O_2$ 154.0994, found 154.0988.

(2*E*,4*E*,6*E*)-2,4,6-Undecatrienyl-2,4-pentadienyl acetate (20). Colorless oil: ^{1}H NMR δ 0.89 (3 H, t, J = 7.0 Hz), 1.24–1.42 (4 H, m), 2.07 (3H, s), 2.10 (2 H, q, J = 7.3 Hz), 4.59 (2 H, d, J = 6.7 Hz), 5.71 (1 H, dt, J = 15.0, 6.7 Hz), 5.75 (1 H, dt, J 15.0, 7.3 Hz), 6.06 (1 H, dd, J = 15.0, 10.4 Hz), 6.10 (1 H, dd, J = 15.0, 10.4 Hz), 6.23 (1 H, dd, J = 15.0, 10.4 Hz), 6.29 (1 H, dd, J = 15.0, 10.4 Hz); ^{13}C NMR δ 13.9, 21.0, 22.2, 31.4, 32.5, 64.9, 125.4, 129.0, 130.0, 134.7, 134.9, 136.7, 170.8; IR

(neat) 1742 cm^{-1} (C=O); HREIMS calcd for $C_{13}H_{20}O_2$ 208.1463, found 208.1488.

(2*E*,4*E*)-3,5-Di(*p*-tolyl)-2,4-pentadienyl acetate (23). Colorless oil: ^1H NMR δ 2.10 (3 H, s), 2.34 (3 H, s), 2.39 (3 H, s)4.95 (2 H, d, *J* = 7.2 Hz), 5.67 (1 H, t, *J* = 7.2 Hz), 6.46 (1 H, d, *J* = 15.9 Hz), 7.13 (2 H, d, *J* = 7.9 Hz), 7.18 (1 H, d, *J* = 15.9 Hz), 7.18 (2 H, d, *J* = 7.9 Hz), 7.24 (2 H, d, *J* = 7.9 Hz), 7.30 (2 H, d, *J* = 7.9 Hz); ^{13}C NMR δ 21.0, 21.2, 21.3, 61.0, 123.6, 123.8, 126.6, 128.7, 128.9, 129.4, 134.2, 134.6, 137.4, 137.9, 138.0, 143.8, 171.0; IR (neat) 1740 cm^{-1} (C=O).

2-Acetoxybiphenyl (3). Colorless crystals: mp 60-62 °C (lit.[6] 63-64 °C); ^1H NMR δ 2.08 (3 H, s), 7.13 (1 H, dd, *J* = 7.9, 1.2 Hz), 7.29-7.42 (8 H, m); ^{13}C NMR δ 20.8, 122.8, 126.4, 127.4, 128.3, 128.5, 128.9, 130.9, 134.9, 137.7, 147.8, 169.3; IR (KBr) 1760 cm^{-1} (C=O); HREIMS calcd for $C_{14}H_{12}O_2$ 212.0837, found 212.0833.

2-Biphenylol. Colorless crystals: mp 55-57 °C (lit.[7] 59-60 °C); ^1H NMR δ 5.19 (1 H, s), 6.98-7.02 (2 H, m) 7.24-7.30 (2 H, m), 7.39-7.51 (5 H, m); ^{13}C NMR δ 115.8, 120.8, 127.9, 128.1, 129.10, 129.14, 129.3, 130.2, 137.1, 152.4; IR (KBr) 3520 cm^{-1} (O-H).

2-Acetoxy-4'-methoxybiphenyl (6). Colorless crystals: mp 84-85 °C; ^1H NMR δ 2.10 (3 H, s), 3.84 (3 H, s), 6.94 (2 H, d, *J* = 8.9 Hz), 7.11 (1 H, dd, *J* = 7.8, 1.4 Hz), 7.27-7.40 (3 H, m), 7.35 (2 H, d, *J* = 8.9 Hz), ^{13}C NMR δ 20.9, 55.2, 113.8, 122.8, 126.4, 128.1, 130.0, 130.8, 134.5, 147.8, 159.1, 169.4; IR (KBr) 1755 cm^{-1}.

2-Acetoxy-2'-chlorobiphenyl (8). Colorless crystals: mp 70-71 °C (lit.[8] 73 °C); ^1H NMR δ 2.00 (3 H, s), 7.20 (1 H, d, *J* = 7.9 Hz), 7.24-7.34 (5 H, m), 7.42-7.48 (2 H, m); ^{13}C NMR δ 20.6, 122.4, 125.8, 126.4, 129.0, 129.2, 129.4, 131.1, 131.4, 132.4, 133.5, 136.3, 148.1, 169.0; IR (KBr) 1760 cm^{-1} (C=O); HREIMS calcd for $C_{14}H_{11}O_2Cl$ 246.0448, found 246.0439.

2-Acetoxy-6-methylbiphenyl (10). Colorless oil: ^{1}H NMR δ 1.87 (3 H, s), 2.12 (3 H, s), 6.95 (1 H, d, *J* = 7.6 Hz), 7.16–7.19 (3 H, m), 7.25–7.41 (4 H, m); ^{13}C NMR δ 20.4, 20.5, 119.7, 127.2, 127.8, 128.0, 128.1, 129.4, 135.0, 136.5, 138.2, 148.5, 169.7; IR (neat) 1765 cm^{-1}; HREIMS calcd for $C_{15}H_{14}O_2$ 226.1005, found 226.0999.

2-Acetoxy-4-methylbiphenyl (12). Colorless oil: ^{1}H NMR δ 2.08 (3 H, s), 2.39 (3 H, s), 6.95 (1 H, s), 7.12 (1 H, d, *J* = 7.6 Hz), 7.30 (1 H, d, *J* = 7.6 Hz), 7.30–7.40 (5 H, m). ^{13}C NMR δ 20.8, 21.0, 123.3, 127.2, 128.2, 128.8, 130.6, 131.9, 137.7, 138.8, 147.6, 169.5; IR (neat) 1762 cm^{-1}.

2-(1-Naphthyl)phenyl acetate. Pale yellow oil: ^{1}H NMR δ 1.75 (3 H, s), 7.24 (1 H, dd, *J* = 7.9, 1.2 Hz), 7.35–7.61 (8 H, m), 7.86–7.90 (2 H, m); ^{13}C NMR δ 20.4, 122.7, 125.1, 125.6, 125.8, 125.99, 126.04, 127.3, 128.05, 128.08, 128.14, 128.8, 131.7, 132.0, 133.41, 133.44, 148.7, 169.3; IR (neat) 1767 cm^{-1} (C=O).

2-(2-Furyl)phenyl acetate (16). Colorless oil: ^{1}H NMR δ 2.37 (3 H, s), 6.48 (1 H, dd, *J* = 3.4, 1.8 Hz), 6.68 (1 H, dd, *J* = 3.4, 0.8 Hz), 7.13 (1 H, m), 7.29 (2 H, m), 7.48 (1 H, dd, *J* = 1.8, 0.8 Hz), 7.82 (1 H, m); ^{13}C NMR δ 21.2, 108.9, 111.7, 123.4, 123.8, 126.3, 127.0, 128.1, 142.2, 146.3, 149.7, 169.0; IR (neat) 1768 cm^{-1}.

***o*-Tolyl acetate (18).** Colorless oil: ^{1}H NMR δ 2.18 (3 H, s), 2.32 (3 H, s), 7.00 (1 H, dd, *J* = 7.9, 1.2 Hz), 7.14 (1 H, td, *J* = 7.4, 1.2 Hz), 7.18–7.24 (2 H, m), ^{13}C NMR δ 16.1, 20.8, 121.9, 126.0, 126.9, 130.1, 131.1, 149.4, 169.2; IR (neat) 1760 cm^{-1}; HREIMS calcd for $C_9H_{10}O_2$ 150.0681, found 150.0690.

3,5-Dimethylphenyl acetate (20). Colorless oil: 2.28 (3 H, s), 2.31 (6 H, s), 6.69 (2 H, s), 6.86 (1 H, s); ^{13}C NMR δ 21.1, 21.2, 119.1, 127.6, 139.3, 150.6, 169.7; IR (neat) 1765 cm^{-1} (C=O); HREIMS calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0853.

(*E*)-2-(1-Hexenyl)phenyl acetate (*E*-22). Colorless oil: ^{1}H NMR δ 0.97 (3 H, t, *J*

= 7.2 Hz), 1.32–1.57 (4 H, m), 2.21 (2 H, q, *J* = 7.0 Hz), 2.33 (3 H, s), 6.22 (1 H, dt, *J* = 15.9, 7.0 Hz), 6.37 (1 H, d, *J* = 15.9 Hz), 7.00 (1 H, dd, *J* = 7.4, 1.8 Hz), 7.18 (1 H, dt, *J* = 7.4, 1.8 Hz), 7.22 (1 H, dt, *J* = 7.4, 1.8 Hz), 7.51 (1 H, dd, *J* = 7.4, 1.8 Hz); ^{13}C NMR δ 13.9, 20.9, 22.2, 31.4, 33.0, 122.5, 123.0, 126.1, 126.6, 127.6, 130.5, 133.9, 147.6, 169.3; IR (neat) 1760 cm^{-1} (C=O); HREIMS calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1291.

(*Z*)-2-(1-Hexenyl)phenyl acetate (*Z*-**22**). Obtained as a mixture with (*E*)-2-(1-Hexenyl)phenyl acetate. ^{1}H NMR δ 0.85 (3H, t, *J* = 7.2 Hz), 1.28–1.57 (4 H, m), 2.15–2.21 (2 H, m), 2.27 (3 H, s), 5.74 (1 H, dt, *J* = 11.7, 7.3 Hz), 6.27 (1 H, d, *J* = 11.8 Hz), 7.04 (1 H, dd, *J* = 7.9, 1.5 Hz), 7.17–7.31 (3 H, m).

6-Methyl-4-(2-*p*-tolylethenyl)-1-naphthyl acetate (**24**). Colorless crystals: mp 137–139 °C; ^{1}H NMR δ 2.38 (3 H, s), 2.48 (3 H, s), 2.53 (3 H, s), 7.08 (1 H, d, *J* = 16.1 Hz), 7.21 (2 H, d, *J* = 8.1 Hz), 7.22 (1 H, d, 7.9 Hz), 7.39 (1 H, dd, *J* = 8.8, 1.7 Hz), 7.49 (2 H, d, *J* = 8.1 Hz), 7.64 (1 H, br s), 7.64 (1 H, d, *J* = 7.9 Hz), 7.76 (1 H, d, *J* = 16.1 Hz), 8.12 (1 H, d, *J* = 8.8 Hz); ^{13}C NMR δ 21.1, 21.3, 21.8, 118.1, 120.4, 122.1, 124.1, 124.3, 126.6, 126.9, 128.8, 129.4, 130.7, 131.7, 133.4, 134.7, 136.1, 137.7, 145.7, 169.6; IR (KBr) 1762 cm^{-1} (C=O); HREIMS calcd for $C_{22}H_{20}O_2$ 316.1463, found 316.1445.

2,4-Di(*p*-tolyl)phenyl acetate (**25**). Colorless crystals: mp 101–102 °C; ^{1}H NMR δ 2.12 (3 H, s), 2.39 (3 H, s), 2.40 (3 H, s), 7.17 (1 H, d, *J* = 8.2 Hz), 7.22–7.26 (4 H, m), 7.36 (2 H, m), 7.49 (2 H, m), 7.54 (1 H, dd, *J* = 8.2, 2.2 Hz), 7.59 (1 H, d, *J* = 2.2 Hz); ^{13}C NMR δ 20.9, 21.1, 21.2, 123.0, 126.8, 127.0, 128.7, 129.1, 129.46, 129.52, 134.7, 135.0, 137.2, 137.3, 137.5, 139.5, 147.0, 169.6; IR (KBr) 1764 cm^{-1} (C=O).

Methyl (3*E*,5*E*)-6-phenyl-3,5-hexadienoate (26). Colorless crystals: mp 46–47 °C; ^{1}H NMR δ 3.19 (2 H, d, 7.3 Hz), 3.70 (3 H, s), 5.89(1 H, dt, *J* = 15.3, 7.3 Hz), 6.30 (1 H, dd, *J* = 15.3, 10.4 Hz), 6.50 (1 H, d, *J* = 15.7 Hz), 6.77 (1 H, dd, *J* = 15.7, 10.4 Hz), 7.21 (1 H, t, *J* = 7.6 Hz), 7.30 (2 H, t, *J* = 7.6 Hz), 7.38 (2 H, d, *J* = 7.6 Hz); ^{13}C NMR δ 38.0, 51.9, 125.5, 126.3, 127.5, 128.3, 128.6, 132.2, 134.0, 137.1, 171.9; IR (KBr) 1732 cm^{-1}; HREIMS calcd for $C_{13}H_{14}O_2$ 202.0993, found 202.1011.

Methyl (2*E*,4*E*)-6-phenyl-2,4-hexadienoate (27). Obtained as a mixture with methyl (3*E*,5*E*)-6-phenyl-3,5-hexadienoate. ^{1}H NMR δ 3.35 (2 H, dd, 7.5, 1.7 Hz), 3.71 (3 H, s), 5.68 (1 H, dt, *J* = 10.7, 7.5 Hz), 6.32 (1 H, m), 6.59 (1 H, d, *J* = 15.6 Hz), 6.97 (1 H, ddd, *J* = 15.6, 11.3, 1.2 Hz), 7.16–7.43 (5 H, m).

References for Chapter 5

1) a) A. Sen and T.-W. Lai, *J. Am. Chem. Soc.*, **104**, 3520 (1982).

b) E. Negishi and J. M. Tour, *Tetrahedron Lett.*, **27**, 4869 (1986).

c) H. Koide, F. Ozawa, and A. Yamamoto, *the 59th Annual Meeting of Chem. Soc., Jpn.*, Abstract 4C442.

d) J. P. Collman, *Acc. Chem. Res.*, **8**, 342 (1975).

e) J. Y. Mérour, J. L. Roustan, C. Charrier, J. Collin, and J. Benaïm, *J. Organomet. Chem.*, **51**, C24 (1973).

2) E. Negishi, G. Wu, and J. M. Tour, *Tetrahedron Lett.*, **29**, 6745 (1988).

3) a) L. Casser, M. Foa, and G. P. Chiusoli, *Organomet. Chem. Syn.*, **1**, 302 (1971).

b) A. Mullen in "*New Syntheses with Carbon Monoxide*", J. Falbe Ed., Springer, Berlin, p.433 (1980).

c) I. Tkatchenko in "*Comprehensive Organometallic Chemistry*", J. Willkinson, F.G.A.Stone, E.W.Abel Eds., Pergamon, Oxford, p.172 (1982).

4) a) S. Murahashi, Y. Imada, Y. Taniguchi, and S. Higashiura, *Tetrahedron Lett.*, **29**, 4945 (1988).

b) L. S. Hegedus and R. Tamura, *Organometallics*, **1**, 1188 (1982).

c) J. Tsuji, K. Sato, H. Okumoto, *J. Org. Chem.*, **49**, 1341 (1984).

5) I. N. Nazarov, L. B. Fisher, *Izv. Akad. SSSR. Otd. Chim.*, 436 (1948).

6) C. F. H. Allen, J. VanAllan, *J. Org. Chem.*, **14**, 798 (1949).

7) O. Kurber, *Ber.*, **81**, 221 (1948).

8) L. Mascarelli, M. Pirona, *Gazz. Chim. Ital.*, **68**, 117 (1938).

Chapter 6

Novel Ketene Formation by Reactions of Acid Chlorides with Low-Valent Platinum Complexes

Abstract

$Pt(CO)_n(PPh_3)_{4-n}$ (n = 0, 1, 2) reacted with $Ph_2CHCOCl$ under CO to afford diphenylketene and *trans*-$PtHCl(PPh_3)_2$. For this reaction, the rate law is zero order in the platinum complex, first order in $Ph_2CHCOCl$, and first order in free PPh_3. A primary isotope effect (k_H/k_D = 4.5) was observed in the reaction of $Ph_2CHCOCl$. A mechanism is proposed which involves the rate-determining enolization of $Ph_2CHCOCl$ by PPh_3 followed by fast abstraction of HCl with a platinum(0) complex.

6–1. Introduction.

As described in Chapters 3 and 4, a possible mechanism of the palladium catalyzed cyclocarbonylation involves a vinylketene intermediate.[1] Furthermore, ketenes and ketene complexes have received increasing attention as important intermediates in transition metal–promoted reactions such as CO hydrogenation[2] and carbonylation of organic or organometallic compounds.[3] A variety of transition metal–ketene complexes have appeared in literatures.[4] Although it is well–known that ketenes can be prepared by treatment of acid halides with bases such as tertiary amines,[5] reactions of low–valent metal complexes with acid halides usually result in the formation of metal acyl complexes instead of ketenes in spite of their basic character. Only a few ruthenium complexes have been reported to give ketenes when reacted with acid chlorides (**Scheme 6.1**).[6,7] However, the reaction mechanism of this dehydrohalogenation has been still ambiguous, although a cationic acylruthenium complex has been proposed as an inter–mediate.

$$Ru(CO)_2(triphos) + CH_3COCl \longrightarrow [RuH(CO)_2(triphos)]Cl + CH_2{=}C{=}O$$

triphos = $CH_3-C(CH_2-PPh_2)_3$

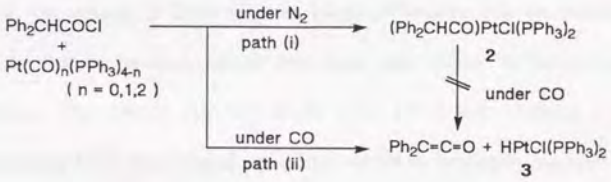
Scheme 6.1 M.C.Baird (1985)

In relation to the study on the reaction mechanism of the cyclocarbonylation, the ketene formation in the presence of palladium and platinum complexes was investigated. In this Chapter, the author wishes to describe the novel diphenylketene formation by the reaction of platinum(0) complexes with diphenylacetyl chloride found in the invetigation.

6–2. Results and Discussion.

When an excess amount of $Ph_2CHCOCl$ was allowed to react with $Pt(PPh_3)_4$ (**1**)

under N_2 in benzene or toluene at r.t., usual oxidative addition occurred to give a colorless acyl complex *trans*-$PtCl(COCHPh_2)(PPh_3)_2$ (**2**).[8] In contrast, when a similar reaction was *conducted under CO*, the color of the solution gradually turned yellow which is characteristic of diphenylketene. Formation of diphenylketene was confirmed by observing a strong absorption[5] at 2100 cm^{-1} in the IR spectrum of the solution, but no absorption due to **2** was observed. The yield of diphenylketene determined by the absorbance at 2100 cm^{-1} attained up to 88% based on **1**, although it could not be isolated because of its instability. Addition of hexane to the reaction mixture afforded *trans*-$PtHCl(PPh_3)_2$ (**3**) in 89%. This result indicates that under CO only the reaction path (ii) proceeds and the usual oxidative addition path (i) is completely suppressed (**Scheme 6.2**).



Scheme 6.2

This type of ketene formation was found to depend largely on the acid chlorides used. Phenylacetyl chloride also reacted with **1** under CO at r.t. to give **3** (68%) and the IR spectrum of the reaction mixture exhibited absorptions at 1905, 1878, and 1710 cm^{-1} indicating the formation of phenylketene dimer.[9] Other acid chlorides such as acetyl chloride, isobutyryl chloride, 2-phenylpropionyl chloride did not react with **1** under CO at r.t., although these chlorides gave the corresponding acyl complexes under N_2. A similar reaction of $Ph_2CHCOCl$ with $Pt[P(OPh)_3]_4$ also produced diphenylketene, but the reaction was very sluggish and therefore not investigated in detail. It should be

mentioned that the ketene formation does not proceed with palladium complexes. Thus, reactions of $Ph_2CHCOCl$ under CO with $Pd(PPh_3)_4$ or $Pd(CO)(PPh_3)_3$ gave only *trans*-$PdCl(COCHPh_2)(PPh_3)_2$, and no diphenylketene was detected by IR.

$$Pt(PPh_3)_4\ (1) \rightleftharpoons Pt(PPh_3)_3 + PPh_3$$
$$Pt(PPh_3)_3 \rightleftharpoons Pt(PPh_3)_2 + PPh_3$$
$$Pt(PPh_3)_3 + CO \rightleftharpoons Pt(CO)(PPh_3)_3\ (4)$$
$$Pt(PPh_3)_2 + 2CO \rightleftharpoons Pt(CO)_2(PPh_3)_2\ (5)$$

Scheme 6.3

Since **1** is known to be in equilibrium with $Pt(CO)(PPh_3)_3$ (**4**) and $Pt(CO)_2(PPh_3)_2$ (**5**) under CO (**Scheme 6.3**)[10], reactions of excess $Ph_2CHCOCl$ with **1**, **4**, and **5** were monitored by measuring the IR absorption at 2100 cm^{-1} at different times. As shown in **Fig. 6.1**, the amount of diphenylketene increased linearly with the reaction time, and this suggests that the reaction rate is zero order with respect to the platinum complex concentration. The reaction rate was in the order **1** > **4** > **5**. Judging from this fact, PPh_3 dissociated from the platinum complexes seems to accelerate the reaction, although no reaction was observed by either ^1H NMR or IR when $Ph_2CHCOCl$ was allowed to stand in contact with PPh_3 in benzene under CO.

In order to clarify the mechanism of this ketene formation, kinetics of the reaction was studied at 29 °C in benzene. When the initial concentration of **1** was fixed, the initial rate was proportional to the initial concentration of $Ph_2CHCOCl$ (**Fig. 6.2**). On the other hand, when the initial concentration of $Ph_2CHCOCl$ was fixed in the presence of a large excess of PPh_3, the initial rate was almost independent of the initial platinum complex concentration (**Fig. 6.3**). Further, under conditions of constant $Ph_2CHCOCl$ and platinum complex concentrations, addition of PPh_3 to the reaction

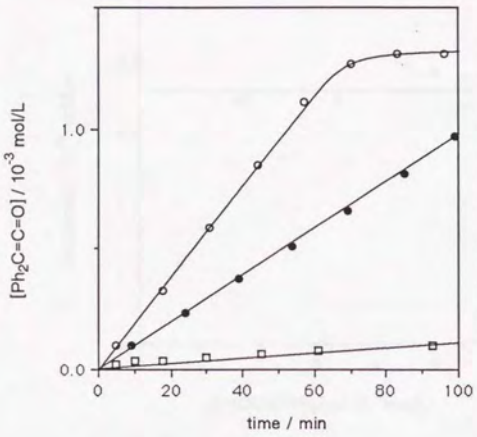


Fig. 6.1
Relation between time and diphenylketene concentration.
Reaction conditions;
$Ph_2CHCOCl$ 0.28 mol/L,
platinum complexes 0.055 mol/L,
in benzene 5 mL, 29 °C, CO 1 atm.

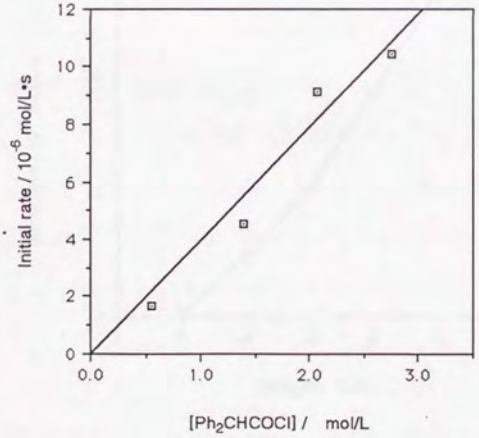


Fig. 6.2
Effect of cocentration of $Ph_2CHCOCl$.
Reaction conditions;
$Pt(PPh_3)_4$ 0.055 mol/L,
in benzene 5 mL, 29 °C, CO 1 atm.

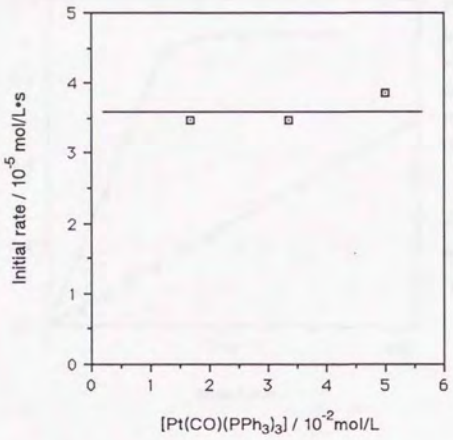


Fig. 6.3
Effect of concentration of platinum complex.
Reaction conditions;
$Ph_2CHCOCl$ 0.24 mol/L,
PPh_3 0.19 mmol,
in benzene 5 mL, 29 °C, CO 1 atm.
Because **4** is the major platinum species in a solution containing excess PPh_3 under CO[11], **4** was used as the platinum the species charged instead of **1** in order to minimize the change of PPh_3 concentration by PPh_3 dissociation.

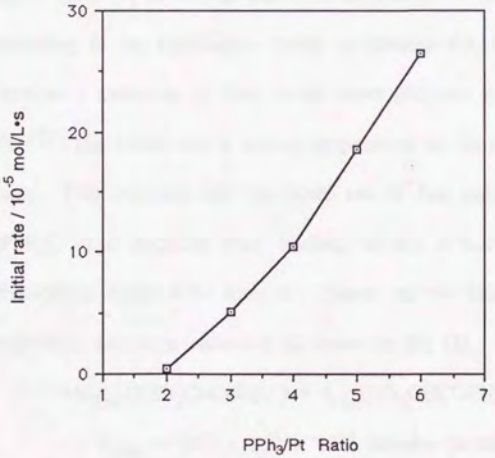


Fig. 6.4
Effect of PPh_3/Pt ratio.
Reaction conditions;
$Ph_2CHCOCl$ 0.28 mol/L,
platinum complexes 0.055 mol/L,
in benzene 5 mL, 29 °C, CO 1 atm.
5, **4**, and **1** were used as the platinum species charged where PPh_3/Pt were 2, 3, and ≥4, respectively.

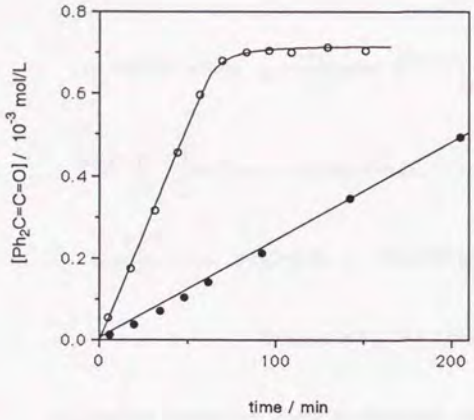


Fig. 6.5
Isotope effect of $Ph_2CDCOCl$.
Reaction conditions;
acid chlorides 0.28 mol/L,
$Pt(PPh_3)_4$ 0.055 mol/L,
in benzene 5 mL, 29 °C, CO 1 atm.

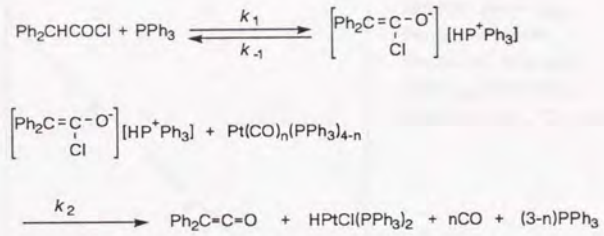
○ $Ph_2CHCOCl$
● $Ph_2CDCOCl$
$k_H / k_D = 4.5$

system clearly increased the rate (**Fig. 6.4**). Unfortunately, the accurate concentration of free PPh_3 could not be determined by ^{31}P NMR because **1** showed only a broad signal under N_2 as well as CO at r.t. on account of fast phosphine exchange. However, according to the equilibrium shown in **Scheme 6.3**, it may be assumed that **4** which contains 3 molecules of PPh_3 is the major platinum species at high PPh_3/Pt ratio under CO.[10] The initial rate is almost proportional to the value (PPh_3/Pt)−3 at high PPh_3/Pt ratio. This indicates that the initial rate is first order in the free PPh_3 concentration [PPh_3]. The deviation from linearity at low PPh_3/Pt ratio is probably due to PPh_3 dissociation from **4** to form **5**. Based on the kinetic data shown above, the rate expression has been estimated as shown in **Eq (1)**.

$$\text{rate}_{obsd.}(d[Ph_2C{=}C{=}O]/dt) = k_{obsd.}[Ph_2CHCOCl][PPh_3] \qquad (1)$$

$$k_{obsd.} = (7.1 \pm 1.2) \times 10^{-4} \text{ L/mol·s (at 29°C)}$$

Furthermore, a primary kinetic isotope effect (k_H/k_D = 4.5) was observed in the reaction of 2-deuteriodiphenylacetyl chloride at 29 °C (**Fig. 6.5**). This suggests that the rate determining step is the C–H bond cleavage in $Ph_2CHCOCl$.



Scheme 6.4 (n = 1 or 2)

A possible mechanism which is consistent with the kinetic data shown above is depicted in **Scheme 6.4**. The first step is the rate determining enolization of $Ph_2CHCOCl$ by PPh_3. Participation of an enol phosphonium salt has been assumed in the diphenylketene formation from bromodiphenylacetyl bromide and PPh_3.[11] Since the reaction of $Ph_2CHCOCl$ with PPh_3 resulted in no change in IR and ^1H NMR as mentioned above, k_1 must be far smaller than k_{-1}. The second step is fast formation of diphenylketene and **3** by the reaction of platinum carbonyl complex $Pt(CO)_n(PPh_3)_{4-n}$ (n = 1 or 2) with the enolized $Ph_2CHCOCl$. Carbonyl ligands diminish the nucleophilicity of the platinum and prevent the oxidative addition of $Ph_2CHCOCl$ giving **2**. However, the platinum complex have the basicity enough to abstract proton from HP^+Ph_3. Subsequent Cl^- abstraction from the $Ph_2CHCOCl$ enolate anion results in the formation of diphenylketene.

The rate equation obtained by applying the steady-state treatment with respect to the enolized $Ph_2CHCOCl$ in **Scheme 6.4** is described as follows.

$$\text{rate}_{\text{calcd.}} = \frac{k_1 k_2 [Ph_2CHCOCl][PPh_3][Pt(CO)_n(PPh_3)_{4-n}]}{k_{-1} + k_2[Pt(CO)_n(PPh_3)_{4-n}]} \qquad (2)$$

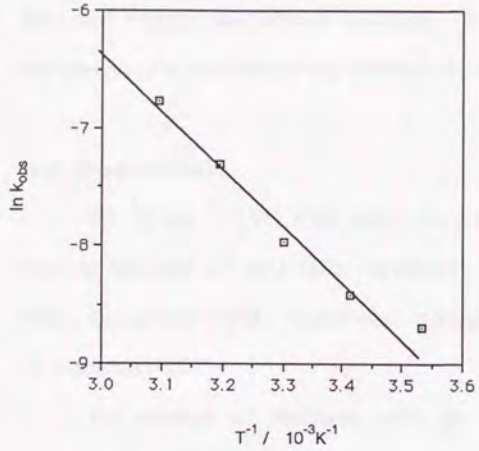


Fig. 6.6
Arrhenius plot of k_{obs}.
Reaction conditions;
$Ph_2CHCOCl$ 0.28 mol/L,
$Pt(PPh_3)_4$ 0.055 mol/L,
in benzene 5 mL, CO 1 atm.

Assuming that $k_2[Pt(CO)_n(PPh_3)_{4-n}] >> k_{-1}$, **Eq (2)** can be approximated as follows.

$$rate_{calcd.} = k_1[Ph_2CHCOCl][PPh_3] \qquad (3)$$

This is in agreement with the observed rate expression **Eq (1)**.

It should be noted that a cationic ruthenium acyl complex was previously considered to be an intermediate in the ketene formation by the reactions of acid chlorides and a ruthenium carbonyl complexes.[6] A mechanism including β-hydrogen elimination of the acyl complex has been proposed. However, in the case of platinum, an acyl complex is unambiguously excluded because the reaction rate is independent of the platinum complex concentration. The fact that **2** did not liberate diphenylketene under CO in benzene also supports the mechanism mentioned above.

Finally, the Arrhenius plot of $k_{obsd.}$ is shown in **Fig. 6.6**, where the equilibrium of **Scheme 6.3** is assumed to be unchanged over the temperature range of 10–50 °C. The overall activation energy was determined to be 11.8 ± 1.4 kcal/mol.

The results described here reveal a novel reactivity of low-valent platinum complexes and provide an important information on the mechanism for ketene formation

from acid chlorides and platinum complexes. Participation of the ketene formation in the catalytic reactions such as the cyclocarbonylation is now under investigation.

6-3. Experimental.

The ^{1}H and $^{31}P\{^{1}H\}$ NMR spectra were recorded on a JEOL GX-400 spectrometer at 400 MHz and 161.8 MHz, respectively. Chemical shifts are relative to internal $SiMe_4$ and external H_3PO_4, respectively. Infrared spectra were taken on a JASCO IR-810 spectrometer.

The reactions are performed under N_2 or CO by Schlenk tube techniques. $Pt(PPh_3)_4$,[11] $Pt(CO)(PPh_3)_3$,[10] $Pt(CO)_2(PPh_3)_2$,[10] $Pt[P(OPh)_3]_4$,[12] $Pd(PPh_3)_4$,[13] $Pd(CO)(PPh_3)_3$[14] were prepared by published methods. Diphenylacetyl chloride, 2-deuteriodiphenylacetyl chloride, and 2-phenylpropionyl chloride were prepared by the reaction of the diphenylacetic acid, 2-deuteriodiphenylacetic acid,[15] and 2-phenylpropionic acid, respectively, with $SOCl_2$.[16] All solvents used were purified by standard methods and stored under N_2 or CO.

Reaction of Acid Chlorides and Platinum or Palladium Complexes.

The following procedure for the reaction of $Ph_2CHCOCl$ with **1** under CO is representative. In a measuring flask was placed a benzene solution (5 mL) of $PhCH_2COCl$ (240 mg, 1.04 mmol) and **1** (343 mg, 0.276 mmol), and the flask was set in a round bottom flask settled in a thermostated oil bath under a CO atmosphere. A small portion of the solution was withdrawn with a syringe every 10-15 min, and diphenylketene in the solution was determined by measuring IR the absorption at 2100 cm^{-1}. The initial reaction rate was determined from the linear part of the time-diphenylketene concentration curve.

In a separate reaction of $Ph_2CHCOCl$ (347 mg, 1.5 mmol) with **1** (623 mg, 0.50 mmol) in toluene (10 mL) under CO for 4 h at r.t., *trans*-$PtHCl(PPh_3)_2$ (**3**)[17] (336 mg, 89 %) was obtained by adding hexane to the reaction mixture: ^1H NMR (CD_2Cl_2) δ −16.19 (t, 1 H, Pt-*H*, ^2J(P-H) = 13.75 Hz, ^1J(Pt-H) = 1195 Hz), 7.4-7.7 (m, 30 H, Ph); $^{31}P\{^1H\}$ NMR δ 28.3 (s, ^1J(Pt-P) = 3012 Hz); IR (KBr) 2220 cm^{-1} (ν(Pt-H)).

A reaction with $Ph_2CHCOCl$ (0.70 mg, 3.0 mmol) with **1** (1.2 mg, 1.0 mmol) in toluene (40 mL) under N_2 gave white precipitate of *trans*-$PtCl(COCHPh_2)(PPh_3)_2$ (**2**) and solution showed no IR absorption due to diphenylketene. After removal of the solvent, recrystallization of the residual solid from CH_2Cl_2-hexane gave *trans*-$PtCl(COCHPh_2)(PPh_3)_2 \cdot \frac{1}{2}(CH_2Cl_2)$ (0.65 g, 65 %) as white crystals. ^1H NMR (CD_2Cl_2) δ 3.15 (s, 1 H, CH_2Ph_2), 6.49-7.74 (m, 40 H, Ph); $^{31}P\{^1H\}$ NMR δ 19.0 (s, ^1J(Pt-P) = 3538 Hz); IR (KBr) 1651 cm^{-1} (ν(C=O)). Anal. Calcd for $C_{50}H_{41}OP_2PtCl \cdot \frac{1}{2}(CH_2Cl_2)$: C, 61.09; H, 4.26. Found: C, 60.88; H, 4.45.

Similarly a reaction of $Ph_2CHCOCl$ (0.90 g, 3.9 mmol) with $Pd(PPh_3)_4$ (1.5 g, 1.3 mmol), in benzene (40 mL) afforded *trans*-$PdCl(COCHPh_2)(PPh_3)_2$ (0.92 g, 82 %) as pale yellow crystals: ^1H NMR (CD_2Cl_2) δ 3.75 (s, 1 H, CH_2Ph_2), 6.62-7.73 (m, 40 H, Ph); $^{31}P\{^1H\}$ NMR δ 18.6 (s); IR (KBr) 1670 cm^{-1} (ν(C=O)).

References for Chapter 6

1 M.Iwasaki, Y.Kobayashi, J.-P.Li, H.Matsuzaka, Y.Ishii, and M.Hidai, *J.Org.Chem.*, in press.

2 a) A.Takeuchi and J.R.Katzer, *J.Phys.Chem.*, **86**, 2438 (1982).

b) E.L.Muetterties and J.Stein, *Chem.Rev.*, **79**, 479 (1979).

c) W.A.Herrmann, *Angew.Chem.,Int.Ed.Engl.*, **21**, 117 (1982).

d) P.T.Wolczanski and J.E.Bercaw, *Acc.Chem.Res.*, **13**, 121 (1980).

3 a) A.Miyashita, T.Kihara, N.Nomura, and H.Nohira, *Chem.Lett.*, 1607 (1986).

b) A.Miyashita, N.Nomura, S.Kaji, and H.Nohira, *Chem.Lett.*, 1983 (1989).

c) T.Mitsudo, H.Watanabe, T.Sasaki, Y.Takegami, Y.Watanabe, K.Kafuku, and K.Nakatsu, *Organometallics*, **8**, 368 (1989).

d) K.H.Dötz In "*Organometallics in Organic Synthesis*", A.de Meijere and H.tom Dieck Eds.;Springer-Verlag, Berlin, 1988, p. 85.

e) W.D.Wulff In "*Advances in Metal-Organic Chemistry*", L.S.Liebeskind Ed; Jai Press Inc., Greenwich, CN, 1988, vol.1, p.209.

4 a) G.L.Geoffroy and S.L.Bassner In "*Advances in Organometallic Chemistry*", F.G.A.Stone and R.West Eds., Academic Press, San diego, 1988, vol.28, p.1.

b) A.Miyashita, *J.Synth.Org.Chem.,Jpn.*, **46**, 135 (1988).

5 R.S.Ward In "*The Chemistry of Ketenes, Allenes and Related Compounds*", S.Patai Ed; Wiley, New York, 1980, Part 1, p. 223.

6 a) S.I.Hommeltoft and M.C.Baird, *J.Am.Chem.Soc.*, **107**, 2548 (1985).

b) S.I.Hommeltoft and M.C.Baird, *Organometallics*, **5**, 190 (1986).

7 S.Singh and M.C.Baird, *J.Organomet.Chem.*, **338**, 255 (1988).

8 C.D.Cook and G.S.Jauhal, *Can.J.Chem.*, **45**, 301 (1967).

9 J.E.Baldwin and J.D.Boberts, *J.Am.Chem.Soc.*, **85**, 2444 (1963).

10 P.Chini and G.Longoni, *J.Chem.Soc., (A)*, 1542 (1970).

11 R.Ugo, F.Caliati, and G.La Monica, *Inorg.Syn.*, **11**, 105 (1968).

12 J.J.Levison and S.D.Robinson, *Inorg.Syn.*, **13**, 109 (1972).

13 D.R.Coulson, *Inorg.Syn.*, **13**, 121 (1972).

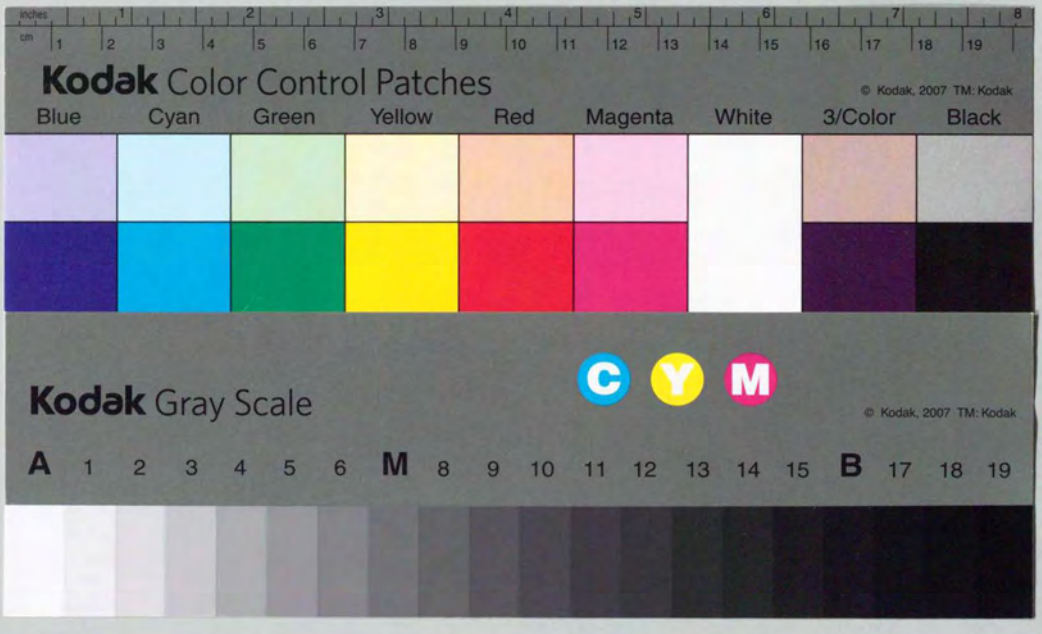
14 K.Kudo, M.Hidai, and Y.Uchida, *J.Organomet.Chem.*, **33**, 393 (1971).

15 J.G.Atkinson, J.J.Csakvary, G.T.Herbert, and R.S.Stuart, *J.Am.Chem.Soc.*, **90**, 498 (1968).

16 H.Staudinger, *Chem.Ber.*, **44**, 1619 (1911).

17 a) J.Chatt and B.L.Shaw, *J.Chem.Soc.*, 5075 (1962).

b) A.F.Clemmit and F.Glocking, *J.Chem.Soc. (A)*, 2163 (1969).


inches
cm
Kodak Color Control Patches
© Kodak, 2007 TM: Kodak
Blue
Cyan
Green
Yellow
Red
Magenta
White
3/Color
Black
Kodak Gray Scale
C
Y
M
© Kodak, 2007 TM: Kodak
A 1 2 3 4 5 6 M 8 9 10 11 12 13 14 15 B 17 18 19