Amino/alkoxycarbonylation of aryl halides mediated by group VI metal carbonyl complexes

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the requirement for the degree of Doctor of Philosophy

2011

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List of Abbreviations

δ	chemical shift (ppm)
$^{\circ}\text{C}$	degree centigrade
Ac	acetyl
aq	aqueous
Ar	aryl (substituted aromatic ring)
atm	standard atmosphere
Bn	benzyl
Bu	butyl
Br	broad singlet
calcd	calculated
cat.	catalytic
cm^{-1}	wave number
d	doublet
dd	doublet of doublets
diglyme	diethylene glycol dimethyl ether
dppe	<i>bis</i> (diphenylphosphino)ethane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DMAP	4-dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
EIHRMS	Electron Ionization High Resolution Mass Spectrometry
eq/equiv	equivalent
ESIHRMS	Electrospray Ionization High Resolution Mass Spectrometry
Et	ethyl

Hz	hertz
IR	infrared spectroscopy
<i>J</i>	coupling constants
LiHMDS	Lithium bis(trimethylsilyl)amide
M	concentration (mol/L)
M ⁺	parent ion peak (mass spectrum)
<i>m</i> -	meta-
m	multiplet
Me	methyl
mg	milligram
MHz	megahertz
mmol	millimole
mp	melting point
NMR	nuclear magnetic resonance
<i>O</i> -	ortho-
O.A.	Oxidative addition
<i>P</i> -	para-
P(<i>o</i> -Tol) ₃	Tris(<i>o</i> -tolyl)phosphine
q	quartet
rt	room temperature
R.E.	Reductive elimination
s	singlet
t	triplet
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography

TMS	trimethylsilyl
Ts	<i>p</i> -toluenesulfonyl

Abstract

Carboxylic amides are a common structure of natural products. Various types of methods for preparation of amides have been reported. The palladium-catalyzed three-component coupling reaction among organic halide, carbon monoxide, and amine is one of the most efficient methods to prepare amides. The reaction proceeds under gaseous carbon monoxide, therefore, it requires a large excess amount of carbon monoxide. The author proposed an alternative method for the palladium-catalyzed amides formation which is a cross-coupling reaction between an organic halide and a carbamoyl metal compound. Although the cross coupling method has an advantage that gaseous carbon monoxide is not required in the reaction, there has been no reports on that so far. The reason why the alternative method has not been studied is due to the lack of useful carbamoyl metal reagents. It was thought that group VI metal carbamoyl complexes, which are known to be easily prepared *in situ* from hexacarbonyl metal with amine in the presence of base, could make the cross-coupling method possible.

It was found that *in situ* generated group VI carbamoyl metal could be applicable for the palladium-catalyzed carbamoylation of aryl halides. Various kinds of amides are prepared in a simple procedure; heating a mixture of aryl halide, tungsten carbonyl amine complex, palladium catalyst, and base in THF (Scheme 1). Gaseous CO-free procedure of the palladium-catalyzed amide synthesis was achieved.

Scheme 1. Palladium-catalyzed carbamoylation of aryl halides by tungsten carbonyl amine complex

During the course of the above experiments, it was found that the amides were obtained even without palladium catalyst when the reaction was performed at higher temperature. Thus, molybdenum and tungsten carbonyl amine complexes played a role of replacement of palladium catalyst (Scheme 2).

Scheme 2. Carbamoylation of aryl halides by molybdenum or tungsten carbonyl amine complexes

Additionally, it was found that *in situ* generation of group VI carbonyl amine complex was applicable for this reaction. When aryl halides were subjected to the reaction with amine in the presence of molybdenum hexacarbonyl in diglyme at 150 °C, the corresponding amides were obtained in good yields (Scheme 3). The carbon monoxide on the molybdenum atom was found to be efficiently incorporated into the product amides. Even though the amount of the molybdenum hexacarbonyl was reduced to 0.167 equivalent which was equal to a stoichiometric amount of carbon monoxide, the reaction still proceeded well. Thus the author found the group VI metal carbonyl complexes acted not only as the carbon monoxide source but also as the catalyst in this reaction. The

reaction is water tolerant and the reaction with aqueous ammonia provided a method for the preparation of primary amide which is difficult to prepare in the conventional three component coupling reaction.

Scheme 3. Mo(CO)₆-mediated carbamoylation of aryl halides

The established methodology was applied to the synthesis of esters simply by changing the nucleophile from amine to alcohol (Scheme 4).

Scheme 4. Mo(CO)₆-mediated alkoxy carbonylation of aryl halides

This group VI metal carbonyl complexes-mediated carbamoylation/ alkoxy carbonylation of aryl halides was applied for the synthesis of heterocyclic compounds. Lactams, lactones, and 3,1-benzoxazin-4-ones were synthesized by simple treatment with molybdenum hexacarbonyl under heating conditions (Scheme 5).

Scheme 5. Applications for Mo(CO)₆-mediated carbamoylation/ alkoxycarbonylation of aryl halides

As stated above, group VI metal carbonyl complexes-mediated carbamoylation/alkoxycarbonylation was developed. The efficiency of the incorporation of carbon monoxide is high and only a little excess of carbon monoxide is necessary as the form of metal carbonyl complexes. The reaction procedure and experimental manipulation are simple.

Chapter 1 General Introduction

Amide and ester groups are fundamentally important in biological systems and commonly found in essential molecules, including major marketed drugs. For example, the amide functional group is an important building unit for caffeine¹ (the most consumed alkaloid compound) (Figure 1–1, **a**), penicillin G² (an antibiotic drug) (Figure 1–1, **b**), piperine³ (isolated from black pepper) (Figure 1–1, **c**), anandamide⁴ (a naturally occurring fatty acid ethanolamide initially isolated from porcine brain) (Figure 1–1, **d**), and atorvastatin⁵ (the top selling drug worldwide since 2003, which blocks the production of cholesterol, also contains amide bond) (Figure 1–1, **e**). Esters are also found as an essential moiety in many natural products and drugs, such as cocaine (a powerful

Figure 1–1. Examples of natural products containing an amide or ester unit

stimulant) (Figure 1–1, **f**), pyrethrin (an insecticide) (Figure 1–1, **g**) and the quinazoline ester (a lipophilic soft drug, which is a very potent inhibitor of dihydrofolate reductase) (Figure 1–1, **h**).⁶

Because of highly important utility of amides and esters in various areas, numerous synthetic methods have been developed.⁷ Traditionally, amides and esters were prepared directly by condensation of carboxylic acids or their activated derivatives with amines or alcohols. This type of reaction is explained as the reaction of an acyl cation equivalent and an *N/O*-nucleophile. The most common method is DMAP-catalyzed condensation in the reaction of carboxylic acid chlorides with amines or alcohols (Scheme 1–1).⁸ For these reactions, a stoichiometric amount of base such as triethylamine is necessary to trap the formed acid.

Scheme 1–1. Amides/esters formation from acyl cation and *N/O*-nucleophile

Amide and ester also can be synthesized by directly condensation of a carboxylic acid with an amine or alcohol (Scheme 1–2).⁹ The equilibrium may be influenced by either removing one product from the reaction mixture (for example, removal of the water by azeotropic distillation or absorption by molecular sieves) or by employing an excess of one reactant.

Scheme 1–2. Formation of amide and ester by condensation of carboxylic acid with amine or alcohol

The alternative methods to synthesize amides and esters can be categorized as follow (Scheme 1–3), (i) reaction of a carbon nucleophile with a carbamoyl or alkoxycarbonyl cation equivalent. (ii) reaction of a carbon electrophile with a carbamoyl or alkoxycarbonyl anion equivalent. (iii) three-component coupling reaction among a carbon electrophile, carbon monoxide, and *N/O*-nucleophile. The merits and demerits for each method are mentioned with examples in the following sections.

Scheme 1–3. Three pathways to form amides or esters

1.1 Amides/Esters Formation by Carbon Nucleophiles and Carbamoyl/Alkoxycarbonyl Cation Equivalents

Amides can be prepared by reacting organometallic reagents with carbamoyl cation equivalents. There are many types of organometallic reagents which can react with carbamoyl cation equivalent to afford amide product. Organolithium reagents,¹⁰

organomagnesium reagents (Grignard reagents),¹¹ organocopper reagents,^{12,13} as well as organotin¹⁴ and arylboronic esters¹⁵ were used as carbanion equivalents to react with carbamoyl chlorides, which were used as the carbamoyl cation counterparts, to afford corresponding amides (Scheme 1–4). The most common carbamoyl chlorides can be prepared by reaction of phosgene with secondary amines under basic conditions. But these methods have several drawbacks. Firstly, due to the sensitivity to water for these organometallic reagents and carbamoyl chlorides, the harsh anhydrous reaction condition was required. Secondly, because carbamoyl chlorides were prepared from phosgene and secondary amines, these reactions can only afford the tertiary amides. Thirdly, phosgene is a gas and difficult to handle due to its toxicity.

Scheme 1–4. Amides formation from organometallic reagents with carbamoyl chlorides

Recently, Kakiuchi et al. reported ruthenium-catalyzed regioselective carbamoylation at aromatic C–H bonds using carbamoyl chlorides.¹⁶ This reaction is unique and useful because organic halides are no longer necessary as the precursors of organometallic reagents. Although carbamoyl chlorides are versatile carbamoyl cation equivalents, they are unstable in the presence of water. The toxicity of phosgene which is the source of carbamoyl chloride is also problematic. Batey et al. developed carbamoyl imidazolium salts, which are stable crystalline materials and used as *N,N*-disubstituted

carbamoyl cation equivalents. The salts which were prepared from commercially available *N,N'*-carbonyldiimidazole (CDI) and amines, can be reacted with different nucleophiles (Scheme 1–5).¹⁷

Scheme 1–5. Preparation of amides with carbamoyl imidazolium salts as the carbamoyl cation equivalent

Indeed, there are also several reports on the Friedel–Crafts type carbamoylation of electron-rich arenes with carbamoyl chlorides in the presence of Lewis acid.¹⁸ A stoichiometric amount of Lewis acid is necessary to activate the carbamoyl chloride to a carbamoyl cation equivalent, and then the aromatic electrophilic substitute occurred to afford the amide (Scheme 1–6).

Scheme 1–6. Preparation of amides from carbamoyl chlorides *via* Friedel–Crafts type carbamoylation

Due to the limitation that only tertiary amides were obtained from carbamoyl chlorides or carbamoyl imidazolium salts as the carbamoyl cation equivalent. Isocyanates were introduced as *N*-monosubstituted carbamoyl cation equivalents, which can react with carbanions to give the secondary amides after the protic work-up (Scheme 1–7).¹⁹

Scheme 1–7.

Similarly, nucleophiles react with alkoxycarbonyl chlorides which were served as alkoxycarbonyl cation equivalents, to produce esters. For example, acetylenic esters are easily synthesized by the reaction of alkynyllithium with alkyl chloroformate (Scheme 1–8).²⁰

Scheme 1–8. Esters formation from alkoxycarbonyl chlorides

Kakiuchi et al not only reported the ruthenium-catalyzed regioselective carbamoylation at aromatic C–H bonds using carbamoyl chlorides, but also reported the alkoxycarbonylations with alkyl chloroformates via aromatic C–H bond cleavage.¹⁶

1.2 Amides/Esters Formation by Carbon Electrophiles and Carbamoyl/ Alkoxy carbonyl Anion Equivalents

1.2.1 General matter

Till now, there are very rare examples of amides or esters formation by the reaction of carbocations with carbamoyl or alkoxy carbonyl anion equivalents. Fukuoka et al. reported that lithium dimethylcarbamoylnickel carbonylate, which was synthesized by the reaction of lithium dimethylamide with nickel carbonyl, could react with organic halides or acetylenic compounds to give the corresponding amides after acidic work-up (Scheme 1–9).²¹

Scheme 1–9. Amides formation from lithium dimethylcarbamoylnickel carbonylate

Corey et al. also reported the alkoxy carbonylation reaction of organic halides by a nickel carbonyl-*t*-butoxide reagent (Scheme 1–10).²² The organic halides are not limited to unsaturated halides, and the alkyl halides can also undergo this alkoxy carbonylation reaction to give the esters. However, this reaction required 6.0 equivalents of Ni(CO)_4 .

Scheme 1–10. Alkoxy carbonylation of organic halides by the nickel carbonyl-*t*-butoxide reagent

1.2.2 Carbamoyl and alkoxy carbonyl group VI metal complexes

As mentioned in section 1.2.1, examples of amide and ester formation by the reaction of carbocations with carbamoyl/alkoxy carbonyl anion equivalents are scarce. The reason why it is so rare is due to the lack of useful carbamoyl/alkoxy carbonyl metals. Carbamoyllithium is one of the most straightforward organometallic reagents for the nucleophilic introduction of carbamoyl moieties into organic compounds, which was used as carbamoyl anion to react with various electrophiles to give the carbamoylation products (Scheme 1–11).²³

Scheme 1–11. Amides formation from carbamoyllithium with carbon cation equivalents

However, there are two main problems for the carbamoyllithium reagents: (i) carbamoyllithiums which bear hydrogen(s) on the nitrogen, were rapidly rearranged to azaenolates of the corresponding formamides; and (ii) carbamoyllithiums which have an

aromatic substituent on the nitrogen, release CO rapidly even at low temperatures (Scheme 1–12). These problems partially prevented its utility in organic synthesis.

Scheme 1-12. Two main problems for carbamoyllithium reagents

In this section, the chemistry of carbamoyl/alkoxycarbonyl group VI metal complexes is introduced. Generally, these complexes were easily prepared by treating amido anions or alkoxides with group VI metal carbonyl complexes (Scheme 1–13).

Scheme 1–13. Generation of carbamoyl/alkoxycarbonyl group VI metal complexes from group VI metal carbonyl complexes

Fischer and co-workers isolated carbamoyl chromium complexes (Scheme 1–14, **A**) from the reaction of lithium diethylamide and chromium hexacarbonyl. The structure was confirmed by X-ray crystallographic analysis after converting it into the ethoxy(amino)carbene complex (Scheme 1–14, **B**).²⁴

Scheme 1–14. Confirmation of the structure of carbamoyl chromium complex

Trautman et al. also reported the reaction of tungsten hexacarbonyl with methoxide (Scheme 1–15).²⁵ The alkoxycarbonyl tungsten complexes were isolated and the structure was determined by NMR, IR and UV analysis.

Scheme 1–15. Formation of alkoxycarbonyl tungsten complexes

Hill et al. reported that divalent tungsten and molybdenum carbamoyl complexes, which serve as precursors for a wide range of bidentate carbamoyl complexes, can be obtained by sequential treatment of $[\text{M(CO)}_6]$ ($\text{M} = \text{W}, \text{Mo}$) with 1 equiv of LiN^iPr_2 , iodine, and PPh_3 , respectively (Scheme 1–16).²⁶

Scheme 1–16. Formation of divalent Tungsten and Molybdenum carbamoyl complexes

McElwee–White et al. reported the synthesis of ureas through oxidative carbonylation of primary amines by using the iodo-bridged tungsten(IV) dimer as the catalyst.²⁷ The mechanism is shown in Scheme 1–17, and the carbamoyl complex **4** was formed by nucleophilic attack of the amine on a carbonyl ligand of **3**, followed by proton abstraction using a second equivalent of the amine. The carbonyl stretching frequency of 2066 cm⁻¹ for **3** falls within the range where nucleophilic attack is expected to occur, indicates the conversion of complex **3** to **4** is reasonable.

Scheme 1–17. Mechanism for the carbonylation of primary amines to ureas

Angelici et al. also reported the generation of carbamoyltungsten intermediates in the reaction of $[(\eta^5\text{-C}_5\text{H}_5)\text{W}(\text{CO})_4]\text{PF}_6$ and methylamine, for which the first step is conversion of $[(\eta^5\text{-C}_5\text{H}_5)\text{W}(\text{CO})_4]^+$ to the carbamoyl complex $(\eta^5\text{-C}_5\text{H}_5)\text{W}(\text{CO})_3(\text{CONHCH}_3)$ followed by reaction of a second equivalent of methylamine (Scheme 1–18).²⁸

Scheme 1–18. Generation of carbamoyltungsten intermediate

As mentioned above, carbamoyl group VI metal complexes were generated by the reaction of group VI metal carbonyl complexes with amines. However, this approach was found to be limited to the thesis of alkoxy(amino)carbene metal complexes,²⁴ ureas²⁹ and formamides.³⁰ These reagents have never been used for C–C bond formation reactions.

1.3 Amides/Esters Formation by Palladium-Catalyzed Three-Component Coupling Reaction

Amide and ester formation by palladium-catalyzed three-component coupling reaction of organic halides, carbon monoxide, and amine or alcohol compounds gives carboxylic acid derivatives, which was first described about 40 years ago by Heck et al.,³¹ is becoming a valuable tool in organic synthesis (scheme 1–19). By this method, amides and esters were catalytically prepared from organic halides and amines or alcohols with one carbon elongation by a simple procedure. Great progress has also been achieved in recent years with regards to catalyst productivity and substrate scope extension.³²

Scheme 1–19. General scheme for the carbonylation of aryl halides

However, a large excess amount of carbon monoxide is necessary for this transformation because the reaction takes place under gaseous carbon monoxide and sometimes high pressure is required. The difficulty in handling of toxic carbon monoxide has created interest in exploring different carbon monoxide equivalents.³³ The ideal carbon monoxide equivalents should be a solid or liquid material which is readily available, and easy to handle. Till now, several carbon monoxide substitutes were developed, such as a mixture of chloroform and aqueous alkali,³⁴ aldehyde,³⁵ formamide,³⁶ dimethylformamide,³⁷ and group VI metal carbonyl complexes. Among these CO equivalents, group VI metal carbonyl complexes are the most widely used due to its stability as a solid and ease of handling. Larhed and co-workers reported a palladium-catalyzed aminocarbonylation reaction of aryl halides by using group VI metal carbonyl complexes as a condensed source of carbon monoxide under microwave irradiation and high reaction temperature (Table 1–1).³⁸ They found that the group VI metal carbonyl complexes are suitable CO-releasing reagents, while other relevant metal carbonyl, such as $\text{Fe}(\text{CO})_5$ and $\text{Co}_2(\text{CO})_8$, did not work well in the aminocarbonylation reaction. The DBU was used as displacing ligand to accelerate the CO releasing, and the reaction time was dramatically shortened by the use of the microwave irradiation. Furthermore, it was found that the palladium-catalyzed aminocarbonylation reactions by using the metal carbonyl as the CO source could be also carried out in water.³⁹ Generally, microwave irradiation, high reaction temperature and around 3 equivalent of DBU are necessary for using group VI metal carbonyl complexes as the CO releasing reagents. These harsh reaction conditions affected their application in organic synthesis to some extent.

Table 1–1. Pd-catalyzed aminocarbonylation by using metal carbonyl as the CO source ^a

entry	metal carbonyl	yield (%)
1	$\text{Cr}(\text{CO})_6$	80
2	$\text{Mo}(\text{CO})_6$	84
3	$\text{W}(\text{CO})_6$	77
4	$\text{Fe}(\text{CO})_5$	0
5	$\text{Fe}_3(\text{CO})_{12}$	0
6	$\text{Co}_2(\text{CO})_8$	28

^a DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene

The general mechanism for the palladium-catalyzed three-component carbonylation reactions is described in scheme 1–20, including the main steps: (i) Oxidative addition of aryl halide to palladium(0) to give arylpalladium(II) intermediate **A**, (ii) migratory insertion of carbon monoxide gives acylpalladium(II) intermediate **B**, (iii) intermediate **B** reacts with amine in the presence of a base to afford the intermediate **C**, (iv) reductive elimination to give the amides or esters with regeneration of palladium(0) catalyst.

Scheme 1–20. General mechanism for the palladium-catalyzed carbonylation reactions

1.4 Perspective for the Thesis

The mechanism of the palladium-catalyzed three-component coupling reaction was discussed in section 1.3. In addition to the mechanism involving the acyl palladium intermediate (scheme 1–21 path A), there is an alternative possible way for this palladium-catalyzed carbonylation reaction (Scheme 1–21, path B).

Scheme 1–21. Reported and hypothetical mechanism of palladium-catalyzed carbonylation of aryl halides

Path B is a cross-coupling reaction between carbamoyl/alkoxycarbonylmetal compounds and organic halides. The key step is the transmetalation between carbamoyl/alkoxycarbonylmetal **C** and palladium(II) intermediate **A** to generate carbamoyl/alkoxycarbonylpalladium(II) intermediate **D**. If the appropriate carbamoyl/alkoxycarbonyl metal intermediate **C** could be generated, after transmetalation between intermediate **C** and arylpalladium intermediate **A**, amide could be formed *via* reductive elimination from the carbamoyl/alkoxycarbonylpalladium intermediate **D**. Although there is the advantage that gaseous carbon monoxide is not necessary, this type of catalytic reaction has never been reported so far. The reason is that useful nucleophilic carbamoyl/alkoxycarbonylation reagents **C** have not been developed.

As discussed in section 1.2.2, the group VI metal carbamoyl/alkoxycarbonyl complexes could be easily prepared by treating amido anions or alkoxides with group VI metal carbonyl complexes. Additionally, it is possible to develop a new synthetic way for

amides/esters synthesis by using the group VI metal carbamoyl/alkoxycarbonyl complexes *via* the pathway which was described in Scheme 1-20, path B. The aim of the proposed work is to combine these two concepts together to test the possibility of the amides/esters formation (Scheme 1-22).

Scheme 1-22. Concept to form amides or esters

Initial investigation was carried out with group VI metal carbonyl amine complexes as carbamoyl metal reagents precursor. As shown in Scheme 1-23, it was expected that group VI carbamoyl complexes **C** would be generated by the combined use of bases and metal pentacarbonyl amine complexes that were known to be easily prepared as air-stable crystalline in most cases.

Scheme 1-23. Generation of carbamoyl metalate

Firstly, tungsten benzylamine complex was used as the carbamoyl tungsten precursor, and was reacted with iodobenzene in the presence of palladium acetate (Scheme 1-24). Fortunately, the desired amide product **3aa** was obtained in 95% yield.

Scheme 1–24. Palladium-catalyzed carbamoylation of phenyl iodide

In chapter 2, the palladium catalyzed carbamoylation of aryl halides by using tungsten carbonyl amine complexes as the carbamoyltungsten precursor was discussed (Scheme 1–25). The scope of the substrates was screened. Then, the palladium-catalyzed intramolecular carbamoylation for lactam synthesis was tested by using tungsten carbonyl amine complexes bearing a 2-iodoaryl moiety as the substrates (Scheme 1–26). Subsequently, the reaction mechanisms were also investigated by experimental studies.

Scheme 1–25. Palladium-catalyzed carbamoylation of aryl halides by using the tungsten amine complexes as the carbamoyltungsten precursor

Scheme 1–26. Palladium-catalyzed intramolecular carbamoylation for the lactam synthesis

In a control experiment in chapter 2, the amide **3aa** was obtained in around 4% yield even without the palladium catalyst (Scheme 1–27). This finding suggested that phenyl iodide could oxidatively add to tungstenate(0) complex although it was not efficient under the reaction conditions. Henceforth, further studies on the possibility of carbamoylation of aryl halides without using palladium catalyst were investigated.

Scheme 1–27. Carbamoylation of aryl halides from tungsten amine complexes without palladium catalyst

In chapter 3, the author documented the findings and developed a carbamoylation reaction in the absence of palladium catalyst. This reaction was optimized by changing the solvent and temperature (Scheme 1–28). It is found that the molybdenum carbonyl amine complexes showed the best yield among the group VI metal carbonyl amine complexes. Different aryl halides were screened as the substrates. Moreover, tungsten ammonia complex was used as the ammonia source to synthesize the primary amides. The carbamoyl molybdenum intermediate was tried to be trapped with norbornene for the mechanism study.

Scheme 1–28. Carbamoylation of aryl halides by molybdenum carbonyl amine complexes

The carbamoylation reaction with molybdenum carbonyl amine complexes was described in chapter 3. It is known that the group VI metal carbonyl amine complexes can be easily prepared from group VI hexacarbonyl complexes (Scheme 1–29). In order to simplify the carbamoylation reaction, it is possible to perform the reaction in one pot way by mixing the amine, aryl halides and $M(CO)_6$.

Scheme 1–29. Formation of molybdenum carbonyl amine complexes

Thus, in chapter 4, a one-pot molybdenum-mediated carbamoylation of aryl halides by directly combining the $Mo(CO)_6$, aryl halides, and amines was described. The carbamoylation reaction only requires near-stoichiometric carbon monoxide in the form of its molybdenum complex, $Mo(CO)_6$ (Scheme 1–30, route A). A wide substrates scope was screened with respect to the aryl halides as well as the amines. Beside carbamoylation reaction of aryl halides with amines, the author extended the nucleophiles to alcohols to achieve the alkoxycarbonylation reaction of aryl halides (Scheme 1–30, route B). Interestingly, the aqueous ammonia and water were used as the nucleophiles to synthesize the primary amides and carboxylic acids, respectively.

Scheme 1–30. Mo(CO)₆-mediated carbamoylation/alkoxycarbonylation of aryl halides

In chapter 5, the author applied the molybdenum-mediated carbonylation reaction for the synthesis of 2-substituted-4*H*-3,1-benzoxazin-4-ones. The Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoanilines with aryl or vinyl halides went smoothly to give the desired products (Scheme 1–31). A wide range of functional groups can be compatible with this reaction condition. The proposed mechanism included double oxidative addition of aryl or vinyl halides to molybdenum center.

Scheme 1–31. Mo(CO)₆-mediated carbonylation reaction to the synthesis of 2-Substituted-4*H*-3,1-benzoxazin-4-ones

Chapter 2 Palladium-Catalyzed Carbamoylation of Aryl Halides by Tungsten Carbonyl Amine Complex

2.1 Introduction

As mentioned in the introduction (Section 1.4, Chapter 1), it was proposed an alternative possible method for the palladium-catalyzed synthesis of amides instead of three-component coupling reaction among aryl halides, carbon monoxide, and amines (Scheme 2-1). That is a cross coupling reaction between organic halides and a carbamoylmatal which would be accomplished by the mechanism including transmetallation with arylpalladium intermediate **A** and the carbamoylmatal **B** giving the aryl(carbamoyl)palladium intermediate **C**, followed by reductive elimination to afford the amide. Concerning the carbamoylmatal for this reaction, it was decided to use group VI transition metal carbonyl complexes because of their acyl derivatives were used in the cross coupling reaction with organic halides as mentioned bellow.

Scheme 2-1. Mechanism of the amide formation from carbamoylmatal intermediate

Narasaka et al. reported that transmetalation between group VI transition metal acyl complexes and palladium catalysts proceeded to give acylpalladium(II) intermediate in the palladium-catalyzed cross coupling reaction between organic halides and acylchromates (Scheme 2–2).⁴⁰ The reaction proceeds smoothly at 50 °C in toluene and gives the arylketone in good yields.

Scheme 2–2. Arylketones formation by the palladium-catalyzed cross coupling reaction between organic halides and acylchromates

This concept of using acylchromates as the acyl anion equivalent in the palladium-catalyzed reaction was expanded for the catalytic arylacylation of alkenes. by mixing aryl iodide, alkene, and acylchromate in the presence of the palladium(0) catalyst gives three-component coupling product in good yields (Scheme 2–3).⁴¹

Scheme 2–3. Arylacylation of alkenes by acylchromate and aryl halides

Acylchromates were proved to be a good acyl donor for the palladium-catalyzed reactions. Most of the acylchromates ammonium salts are stable solid in the air and can be easily prepared in the reaction of chromium hexacarbonyl with organolithium reagents.

In the same manner as for the preparation of the acylmetal complexes, it is known that group VI carbamoyl complexes are easily generated in the reaction of metal carbonyl complexes and metal amides as explained in chapter 1 section 1.2.2. Inspired by the utility of group VI acylmetalates, it was decided to use group VI carbamoylmetalates for the palladium-catalyzed cross coupling reaction with organic halides to prepare amides. Firstly, the author tried to isolate carbamoylmetal complexes in the reaction of metal hexacarbonyl and lithium amide, however, they were found to be thermally unstable and could not be isolated in the pure form. Therefore, it was decided to use in situ generation of carbamoylmetal species for the palladium-catalyzed cross coupling reaction. For the precursor of the carbamoylmetalate, the metal pentacarbonyl amine complexes were selected as depicted in Scheme 2-4. The reason to choose these complexes is that acylmetalates are more easily generated from the coordinatively unsaturated carbonyl complexes with relatively weaker organometallic reagents such as organozinc compounds compared to the reaction of hexacarbonylmetal with organolithium as shown in Scheme 2-5.⁴²

Scheme 2-4. The group VI metal carbonyl amine complexes were used as the precursor of carbamoylmetal reagents

Scheme 2-5. Acylchromium formation from coordinatively unsaturated carbonyl complexes with organozinc compounds

2.2 Results and Discussion

2.2.1 Preparation of the Group VI Metal pentacarbonyl Amine Complexes

The group VI metal pentacarbonyl benzylamine complexes **2** [(OC)₅MNH₂CH₂Ph; M = Cr, Mo, W] were prepared in 2 steps from the corresponding hexacarbonyl metal complexes.^{43,44} Chlorometalates ammonium salts **1a–1a''** were obtained in excellent yields by heating a mixture of the hexacarbonyl metal with tetraethylammonium salt in diglyme (diethylene glycol dimethyl ether). The ligand exchange with benzylamine gives the corresponding amine complexes **2a–2a''** in 38–73% yields (Scheme 2–6). These metal carbonyl benzylamine complexes are air-stable crystallines in most cases.

Scheme 2–6. Preparation of group VI metal carbonyl amine complexes

2.2.2 Palladium-Catalyzed Carbamoylation of Phenyl Iodide

With the amine complexes in hand, an investigation of the palladium-catalyzed carbamoylation of aryl halides was next carried out. Firstly, iodobenzene was selected as

the coupling partner. To a mixture of the tungsten benzylamine complex **2a** (0.50 mmol) and base (0.55 mmol) in THF, iodobenzene (0.75 mmol), Pd(OAc)₂ (0.025 mmol), and P(*o*-Tol)₃ (0.05 mmol) were added and the reaction mixture was heated to reflux (Scheme 2–7).

Scheme 2–7. The first attempt of the palladium-catalyzed carbamoylation of phenyl iodide

Firstly, LiHMDS was used as the strong base to generate lithium benzylamide completely. The reaction was completed in 2 h and benzamide **3aa** was obtained in 70% yield. It was found that the use of a weaker base, K₂CO₃, gave an excellent yield (95%) although a longer reaction time was required. In both cases a small amount of biphenyl (<3%) was obtained as a side product. Carbamoylation of iodobenzene was also performed by using other group VI metal benzylamine complexes **2a'** and **2a''**. Molybdenum complex **2a'** gave a good yield of **3aa**. However, chromium complex **2a''** gave only 39% yield. In this work, method **A** uses K₂CO₃ as the base and method **B** uses LiHMDS as the base.

When a control reaction was performed without Pd(OAc)₂ and P(*o*-Tol)₃ (Scheme 2–8), amide **3aa** was obtained in <4% as a mixture of undefined compounds and

benzylamine complex **2a** was recovered in 42%. This provided evidence that amides formation is of less efficiency without palladium acetate.

Scheme 2–8. Carbamoylation of aryl halides from tungsten amine complexes without palladium catalyst

2.2.3 Scope and Limitation of the Carbamoylation

Palladium-catalyzed carbamoylation of a variety of aryl halides by method **A** was performed and the results are summarized in Table 2–1. It was found that not only aryl iodides but bromide counterparts could be used as the coupling partners although longer reaction time and a higher catalyst loading (10 mol%) was required. The higher reactivity of the iodide was further demonstrated proven by reaction of 1-bromo-4-iodobenzene undergoing a chemoselective carbamoylation to afford 4-bromobenzamide **3ea** in good yield (entry 7). Functional group tolerance was tested by using 4-substituted phenyl halides and it was found that vinyl, ethoxycarbonyl, and methoxy groups were not affected under the reaction conditions (entries 8–10). However, when a substrate containing an acyl group was treated with this reaction condition for long time, it was partially reduced to the hydroxyl group (entry 4). This reaction was also applicable for the catalytic carbamoylation of heteroaromatic halides; 3-thiophenecarboxamide **3ia** was obtained from 3-bromothiophene in 63% yield (entry 11).

Table 2–1. Palladium-catalyzed carbamoylation of aryl halides with K₂CO₃ (method A)^a

entry	Ar-X	product	time/h	yield/%
1	1a	3aa	16 72 ^b	95 (<4) ^{b,c}
2	1a'	3aa	72	47
3	1b	3ba	16	95
4	1b'	3ba R = 3ba' R =	60	74 ^d
5	1c	3ca	68	86
6	1d	3da	70	81

Continued

7			13	84
8			48	63
9			84	64
10			16	95
11			72	63

^a Reaction conditions of Method A: a mixture of **2a** (0.5 mmol), Ar-X (0.75 mmol), K₂CO₃ (0.55 mmol), Pd(OAc)₂ (5 mol % for aryl iodide, 10 mol % for aryl bromide), and P(o-Tol)₃ (10 mol % for aryl iodide, 20 mol % for aryl bromide) in THF was heated to reflux under N₂ till the reaction was finished.

^b Without Pd(OAc)₂ and P(o-Tol)₃.

^c **2a** was recovered in 42%.

^d **3ba** and **3ba'** were obtained in 63% and 11% yields, respectively.

In addition, by using LiHMDS as the base (method **B**) to perform the carbamoylation, the reaction time could be shortened. Thus the author tried to make a comparison of the difference between the two methods. The results for the palladium-catalyzed carbamoylation of aryl halides by using LiHMDS as the base are summarized in Table 2–2. Overall, the reaction time was approximately reduced by half but with lower product yields. In contrast, for some aryl bromide substrates, such as the bromobenzene and 3-bromothiophene, higher product yields were obtained by using LiHMDS as the base (entries 2 and 11). It is noteworthy that phenyl triflate can be used as the electrophile substrate for this protocol, although the yield is low (entry 3). Interestingly,

the benzyl bromide was converted to the amide product **3ka** in good yield even without the palladium catalyst and the ligand (entry 13).

Table 2–2. Pd-catalyzed carbamoylation of aryl halides with LiHMDS (method B)^a

entry	Ar-X	product	reflux time/h	yield/%
1	1a	3aa	5	78
2	1a'	3aa	30	72
3	1a''	3aa	24	23 ^b
4	1b'	3ba	24	54
5	1c	3ca	30	84
6	1d	3da	20	71
7	1e	3ea	12	85
8	1f	3fa	12	67
9 ^c	1g	3ga	14	69

Continued

10		1h	3ha	12	75
11		1i	3ia	8	72
12		1j		12	45
13 ^d		1k		20	76

^a Reaction condition of method B is: LiHMDS (0.55 mmol) was added to a mixture of **2a** (0.5 mmol), Ar-X (0.75 mmol), Pd(OAc)₂ (5 mol %), P(o-Tol)₃ (10 mol %) in THF at -78 °C, warm to rt, then heated to reflux under N₂ till the reaction was finished.

^b Recovery of **2a**: 27%.

^c 5 mol % Pd(OAc)₂, 10 mol % dppe.

^d Without Pd(OAc)₂ and ligand.

2.2.4 Palladium-Catalyzed Intramolecular Carbamoylation

The palladium-catalyzed amide preparation was successful with tungsten carbonyl amine complexes. Then the application of the reaction conditions to the intramolecular cyclization was next examined. Firstly, substrates for the intramolecular carbamoylation reaction, tungsten amine complexes **2b** and **2c**, were prepared according to the reported literatures outlined in Scheme 2–9.⁴⁵ Both are air-stable yellow solid compounds.

Scheme 2–9. Preparation of tungsten amine complexes **2b** and **2c**

Next, the two tungsten amine complexes **2b** and **2c** having a 2-iodoaryl moiety were subjected to the palladium-catalyzed reaction by using both K_2CO_3 and LiHMDS (Scheme 2–10). Intramolecular carbamoylation proceeded to give the 5- and 6-membered ring lactams **3b** and **3c** for both methods. Obviously, compared with the reaction with K_2CO_3 , the use of LiHMDS gave higher yields and shorter reaction time.

Scheme 2–10. Palladium-catalyzed intramolecular carbamoylation

2.2.5 Mechanistic Investigations

As stated in the introduction (Section 1.4, Chapter 1), there are two possible mechanisms for the palladium-catalyzed amide formation. If amine and carbon monoxide are released from the tungsten center in the reaction conditions, the two mechanisms cannot be distinguished. To gain some insight into the mechanism of this palladium-catalyzed carbamoylation, the carbamoylation reaction under the atmospheric pressure of carbon monoxide without using tungsten carbonyl complexes was examined. If the tungsten complex was used only as the carbon monoxide source in Path A, the amide would be obtained under the CO atmosphere without the tungsten carbonyl complex. The palladium-catalyzed reaction was performed with the combination of benzylamine and carbon monoxide (1 atm) instead of using the tungsten carbonyl amine complex (Scheme 2–11). When 2-bromonaphthalene (**1c**) was subjected to the reaction, the corresponding amide **3ca** was not obtained even under refluxing conditions for 36 hours. The reaction seems to require higher temperature or higher pressure of carbon monoxide to accomplish amide formation via path A (Scheme 2–12). In contrast, the tungsten carbonyl benzylamine complex gave the amide in 84% yield. Although the possibility of path A cannot be completely excluded, these results suggested the reaction proceeds via path B, in which transmetalation of carbamoylmatalate occurs.

Scheme 2–11. Carbamoylation of aryl halide with different CO source

Scheme 2-12. Reported and hypothetical mechanism of palladium-catalyzed carbamoylation of aryl halides

The main difference between path A and B is whether the reaction proceeds via acylpalladium intermediate (path A) or carbamoylpalladium intermediate (path B). So, the palladium-catalyzed reaction in the presence of reactive alkene to trap the palladium intermediates was performed (Scheme 2-13). When norbornene was added to the palladium-catalyzed reaction of iodobenzene, the phenylcarbamoylation product **4** was obtained in 46% yield as a mixture of *syn* and *anti* stereoisomers along with benzamide **3aa** and a small amount of 2-carbamoylnorbornane **5**. Yamane and co-workers reported *cis-exo* addition in palladium-catalyzed arylacylation of norbornene (Scheme 2-14).⁴¹ Thus, if the reaction proceeds via phenylpalladation of norbornene followed by reductive elimination, *cis-exo* stereoisomer should be obtained. The mechanism of the formation of *trans*-stereoisomer of **4** and 2-carbamoylnorbornane **5** is not clear at this stage. The fact that not the benzoyl- but the carbamoylnorbornene was obtained suggests that the

reaction proceeds via carbamoylpalladium intermediate (path B) although there is still a possibility to form product **4** via CO insertion to norbornarylpalladium intermediate.

Scheme 2–13. Using norbornene to trap the palladium intermediate

Scheme 2–14. Mechanism of palladium-catalyzed arylacylation of norbornene

2.3 Conclusion

In summary, the palladium-catalyzed carbamoylation of aryl halides was accomplished by using tungsten(0) carbonyl amine (Scheme 2–15, eq. a). Various aryl halides can be applied to this reaction. The synthesis of the lactams was also achieved *via* the intramolecular carbamoylation (Scheme 2–15, eq. b). The carbamoylation reaction may involve transmetalation between carbamoylmatalate and palladium(II) intermediate. This reaction can be performed without using gaseous carbon monoxide and may provide an alternative method of conventional palladium-catalyzed three-component coupling reaction of aryl halide, carbon monoxide, and amine.

Scheme 2–15. Palladium-catalyzed carbamoylation of aryl halides by tungsten carbonyl amine complexes

Chapter 3 Carbamoylation of Aryl Halides by Molybdenum or Tungsten Carbonyl Amine Complexes

3.1 Introduction

The palladium-catalyzed carbamoylation of aryl halides by tungsten carbonyl amine complexes was described in chapter 2. The carbamoylation reaction proceeded smoothly to give the amides in good yields. From the result of the reaction without the palladium catalyst, it was clear that the palladium catalyst played a significant and indispensable role in the reaction. The yield of *N*-benzylbenzamide was only less than 4% even after refluxing in THF for 72 hours without palladium catalyst, and a similar result was found when 3-bromothiophene was used in place of phenyl iodide (Scheme 3–1). From another view point, this reaction may also take place even without the presence of palladium catalyst as a detectable amount of product was isolated. This means that there is a possibility that the tungsten carbonyl amine complex acts not only as the source of the amino and carbonyl group, but also as the catalyst instead of the palladium complex.

Thus, it became interesting to find out if the formation of amide could be achieved in the absence of palladium catalyst. The mechanism of this amide formation may include two possibilities (Scheme 3–2). One pathway includes the following steps: the carbamoyltungsten intermediate **A** was first formed in the presence of base, then, oxidative addition of phenyl iodide to tungsten center to give intermediate **B**, followed by reductive elimination to give the amide **3aa**. Alternatively, oxidative addition of phenyl iodide to the tungsten of **2a** affords the phenyltungsten intermediate **C**, which is subjected to CO insertion to C–W bond to give the benzoyltungsten intermediate **D**, which then yields, after reductive elimination, the amide **3aa**.

Scheme 3–1. Comparison of the carbamoylation of aryl halides with and without palladium catalyst

Scheme 3–2. Two possible mechanisms for the carbamoylation of iodobenzene without palladium catalyst

As described, the formation of amides in the absence of the palladium catalyst is explained by the mechanism including the oxidative addition of aryl halide to the tungsten complex. There are some reports on similar oxidative additions. Richmond et al reported that the aryl carbon–halogen bonds of potentially tetradentate ligands **A** (X = Cl, Br, I) are readily cleaved by reaction with W(CO)₃(RCN)₃ to afford seven-coordinate tungsten(II) complexes **B** (Scheme 3–3).⁴⁶ Later, Richmond et al reported another similar chelate-assisted oxidative addition of carbon–halogen bond to tungsten center (Scheme 3–4).⁴⁷ These examples have demonstrated that facile chelate assisted oxidative addition of

carbon–halogen bonds, although it is limited to specific aryl halides bearing a chelating group.

Scheme 3–3. Seven-coordinate tungsten(II) complexes formation by chelate-assisted oxidative addition of carbon–halogen bond to tungsten

Scheme 3–4. Seven-coordinate tungsten(II) complexes formation by chelate-assisted oxidative addition of carbon–halogen bond to tungsten

Iwasawa et al also reported that aryl halides oxidatively added to low valent molybdenum complex at 160 °C in DMF and acylmolybdenum intermediate **A** was formed in the acylation of alkenes (Scheme 3–5).⁴⁸

Scheme 3–5. Intermolecular addition reaction to alkenes of acylmolybdenum complexes

Later, Iwasawa et al developed a unique molybdenum-promoted carbonylative cyclization of *o*-haloaryl and β -haloalkenylimines leading to γ -lactam derivatives (Scheme 3–6).⁴⁹ The mechanism of this reaction was proposed as follows: firstly, aldimine-assisted oxidative addition of aryl iodide to coordinatively unsaturated Mo(CO)_n , which is generated by the dissociation of carbonyl ligands under the reaction conditions, occurs to afford an arylmolybdenum(II) intermediate **A**. The successive insertion of a carbonyl ligand generates acyl molybdenum complex **B** and insertion of the C=N bond occurs to afford an alkyl molybdenum intermediate **C**. Finally, transmetalation and reductive elimination of intermediate **C** gives the dimeric isoindolinone, whereas protonation of intermediate **C** by the water present in DMF affords the monomer as a minor product. These examples of oxidative addition of aryl halides to group VI transition metal supported our hypothesis: carbamoylation of aryl halides without the palladium catalyst.

Scheme 3–6. Molybdenum-promoted carbonylative cyclization of *o*-haloaryl and β -haloalkenylimines leading to γ -lactam derivatives

3.2 Results and Discussions

3.2.1 Carbamoylation of Phenyl Iodide by Molybdenum Carbonyl

Amine Complexes

Previous finding, in which the formation of a trace amount of the amide suggested that a tungsten(0) intermediate could be a substitute for the palladium catalyst, encouraged the author to develop the carbamoylation of aryl halide mediated by group VI metal carbonyl amine complex. Because the reaction temperature of THF at reflux did not seem to be high enough, diglyme was selected as the solvent for the carbamoylation reaction. The effect of the temperature for this reaction was tested using iodobenzene with tungsten carbonyl amine complex **2** in the presence of Bu_3N as the base (Table 3–1).

At 100 and 120 °C, the desired product was obtained in very low yields after heating for about 20 hours (entries 1 and 2). However, when the reaction temperature was increased to 150 °C, the yield was dramatically increased up to 75% after heating for only 3 hours (entry 3).

Table 3–1. Carbamoylation of iodobenzene with tungsten carbonyl amine complexes^a

$\text{PhI} + \text{Ph}-\text{CH}_2-\text{N}(\text{H})_2-\text{W}(\text{CO})_5 \xrightarrow[\text{diglyme, Tem. Time}]{n\text{Bu}_3\text{N (1.1 eq.)}} \text{Ph}-\text{C}(=\text{O})-\text{N}(\text{H})-\text{CH}_2-\text{Ph}$

1a **2a** **3aa**

entry	temperature/°C	time/h	yield of 3aa / % ^b	recovery of 2 / %
1	100	20	6	33
2	120	18	6	27
3	150	3	76	0

^a Reaction conditions: The mixture of **1a** (0.75 mmol), **2a** (0.5 mmol), *n*Bu₃N (0.55 mmol) in diglyme was heated under N₂ atmosphere.

^b Isolated yield.

Different bases were also subjected to the reaction system and the results are summarized in Table 3–2. Inorganic bases such as K₂CO₃ and LiHMDS afforded relatively lower yields (entries 1 and 2). The organic base *n*Bu₃N was found to be the best for this carbamoylation reaction (entry 4).

Table 3–2. Carbamoylation of iodobenzene with different bases^a

<div><div><div><div><div>PhI</div><div>1a</div></div><div>+</div><div><div><div>Ph</div><div><div><div>N</div><div>H₂</div></div><div>W(CO)₅</div></div></div></div><div><div>base (1.1 eq.)</div><div>diglyme, 150 °C</div></div><div><div><div>Ph</div><div><div><div>O</div><div>C=O</div></div><div>N</div><div>H</div></div><div>Ph</div></div></div></div></div></div>			
entry	base	time/h	yield of 3aa / % ^b
1	K ₂ CO ₃	2	53
2	LiHMDS	4	22
3	Et ₃ N	3	68
4	ⁿ Bu ₃ N	3	76
5	DBU	6	63

^a Reaction conditions: The mixture of **1a** (0.75 mmol), **2a** (0.5 mmol), ⁿBu₃N (0.55 mmol) in diglyme was heated under N₂ atmosphere.

^b Isolated yield.

Next, the reactivity of the other group VI metal carbonyl amine complexes were investigated (Table 3–3). The corresponding molybdenum complex was found to provide an excellent yield of amide (entry 2), and a comparable yield was obtained even at 120 °C (entry 3). This suggested that the molybdenum complex is more reactive than the tungsten complex in this reaction system. On the other hand, the chromium complex gave only a trace amount of the product (entry 5).

Table 3–3. Carbamoylation of iodobenzene with different group VI metal carbonyl amine complexes^a

$\text{PhI} + (\text{OC})_5\text{M}-\text{N}(\text{H}_2)\text{CH}_2\text{Ph} \xrightarrow[\text{diglyme, temp., time}]{n\text{Bu}_3\text{N}} \text{Ph}-\text{C}(=\text{O})-\text{N}(\text{H})\text{CH}_2\text{Ph}$

1a **2** **3aa**

entry	M (2)	temperature/°C	time/h	yield of 3aa /%
1	W 2a	150	3	76
2	Mo 2a'	150	1	97
3	Mo 2a'	120	1	95
4	Mo 2a'	90	20	6
5	Cr 2a''	150	3	trace

^a Reaction conditions: The mixture of **1a** (0.75 mmol), **2** (0.5 mmol),

*n*Bu₃N (0.55 mmol) in diglyme was heated under N₂ atmosphere.

^b Isolated yield.

3.2.2 Scope and Limitation of the Carbamoylation

With the optimized reaction conditions in hand, the scope of the reaction was investigated by testing various kinds of aryl halides (Table 3–4). The reactions were carried out with 1:1.2 ratio of molybdenum carbonyl benzylamine complex and aryl halide in the presence of 1.1 molar amount of tributylamine as the base. The reaction was not only limited to aryl iodides, but aryl bromides could also be applied for this carbamoylation reaction without diminishing the yields (entries 1–5). When 1-bromo-4-iodobenzene was used as the substrate, selective carbamoylation product, 4-bromobenzamide **3ea**, was obtained (entry 6). Both electron-deficient and -rich aryl halides gave good yields (entries 7–11). Regardless of the substitution pattern, *ortho*-, *meta*-, and *para*-, iodo(methoxy)benzenes gave the corresponding amides in good yields

(entries 9–11). Not only the aryl but also the heteroaryl halides could be applied although 2-bromopyridine gave the product in a low yield (49%) (entries 12 and 13). Benzyl and alkenyl bromides were also applicable to this reaction to obtain 2-phenylacetoamide **3ka** and α,β -unsaturated amide **3oa** respectively (entries 14–15). All reactions were completed within 3 hours, in contrast to the fact that palladium-catalyzed carbamoylation of aryl halides with tungsten carbonyl amine complexes requiring longer reaction time which was discussed in Chapter 2.

Table 3–4. Carbamoylation of organic halides by $(\text{CO})_5\text{MoNH}_2\text{Bn}^a$

$ \begin{array}{c} \text{Ar-X} + (\text{OC})_5\text{MoN} \begin{array}{c} \text{CH}_2\text{Ph} \\ \\ \text{H}_2 \end{array} \xrightarrow[\text{diglyme, 120–150 } ^\circ\text{C,}]{^n\text{Bu}_3\text{N (1.1 equiv)}} \text{Ar} \begin{array}{c} \text{O} \\ \\ \text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_2\text{Ph} \\ \\ \text{H} \end{array} \\ \text{1} \qquad \qquad \text{2a'} \qquad \qquad \qquad \text{Time} \qquad \qquad \qquad \text{3} \end{array} $				
entry	Ar-X	product	time/h	yield/%
1	1a	3aa	1	95
2	1c'	3ca	1	95
3	1d'	3da	1	87
4	1c	3ca	1	92
5	1d	3da	1	87

continued

6	1e	3ea	0.5	75
7	1l	3la	3	89
8	1g	3ga	3	88
9	1h	3ha	1.5	95
10	1m	3ma	1	80
11	1n	3na	1	88
12	1i	3ia	1.5	91
13	1j	3ja	1	49
14	1k	3ka	1	78
15	1o	3oa	1	93

^a Reaction conditions: a mixture of **1** (0.6 mmol), **2a'** (0.5 mmol), ⁿBu₃N (0.55 mmol) in diglyme was heated under N₂.

When the electron-deficient alkenyl bromide (*Z*)-ethyl 3-bromoacrylate was used as the substrate, the α , β -unsaturated amide **3pa** was obtained. However, the amide product **3pa** was easily reduced to amide **3pa'** under this reaction condition if the reaction time was increased (Scheme 3–7).

Scheme 3–7. Carbamoylation of (*Z*)-ethyl 3-bromoacrylate

Next, the scope of amine complexes for this reaction was investigated (Scheme 3–8). Tungsten ammonia complex **2d** was easily prepared from $(OC)_5WClNEt_4$ with aqueous ammonia solution.⁵⁰ When the ammonia complex **2d** was subjected to phenyl iodide, *N*-nonsubstituted benzamide **3ad** was obtained in 40% yield. Although the yield is not excellent, the result is noteworthy because preparation of primary amides by conventional palladium-catalyzed three-component coupling reaction is still fraught with difficulties.⁵¹ The procedure is not practical because it requires to use hazardous ammonia gas at high temperature. Primary amine **2e** substituted by a primary alkyl group gave an excellent yield of amide **3ae** (98%). Cyclic secondary amine complex **2f** was also applicable for this reaction and *N*-benzoylpyrrolidine **3af** was obtained in 91% yield.

Scheme 3–8. Carbamoylation of iodobenzene with some molybdenum amine complexes

3.2.3 Mechanistic Investigations

Although the mechanism for the carbamoylation reaction is still unclear, two possibilities must be taken into consideration in a similar manner as we discussed in Chapter 2, Section 2.2.5. As shown in Scheme 3–9, one involves generation of acyl metal intermediate **X** and the other is generation of carbamoyl metal intermediate **Y**. Acyl metal intermediate **X** would be generated by the oxidative addition of aryl halide to molybdenum complex **E**, followed by insertion of carbon monoxide to the acyl-molybdenum bond. Iwasawa and co-workers reported that aryl halides oxidatively added to low valent molybdenum complex at 160 °C in DMF and an acylmolybdenum intermediate was formed in the acylation of alkenes.³ Carbamoyl metal complex **Y** would be generated from arylmetal amide **F**, or from carbamoyl metalate **G** by oxidative addition of aryl halides. Although it is known that heteroatoms such as RO^- and R_2N^- on transition metals rarely migrate to carbon monoxide to form alkoxycarbonyl or carbamoyl metals,⁵² the possibility of this mechanism involving carbamoyl metal intermediate still cannot be excluded.

Scheme 3–9. Proposed mechanism of carbamoylation of aryl halides

To confirm the formation of tetracarbonyl complex **H**, the author tried to trap it as a complex with a bidentate ligand. When 1.0 equivalent of dppe was added after the reaction, $(\text{OC})_4\text{Mo}(\text{dppe})$ (**6**) was isolated in 74% yield (Scheme 3–10). This means that in this reaction, **2a'** efficiently converted one of its CO into the amide product, there still left four CO around the molybdenum.

Scheme 3–10. Attempt to trap the molybdenum intermediate by dppe

To gain some insights on the mechanism of the reaction, the reactions in the presence of reactive alkenes was tested. If the alkene could trap the organometallic intermediate, it could determine which mechanism depicted in Scheme 3–9 is correct, either the acylmolybdenum- or carbamoylmolybdenum-involving mechanism. Iwasawa et al reported that the acylmolybdenum intermediate was generated and aroylation of alkene proceeded when iodobenzene was reacted with ethyl acrylate in DMF at 160 °C as shown in Scheme 3–5.³ When the reaction was performed with molybdenum carbonyl benzylamine complex in the presence of methyl acrylate, the aroylation product **7** was obtained in 28% yield along with benzamide **3aa** in 72% yield, and no carbamoylation of the acrylate took place (Scheme 3–11). Although the yield of the aroylation product **7** was low, this finding supports the mechanism involving the acylmolybdenum intermediate **X**.

Scheme 3–11. Attempt to trap the molybdenum intermediate by acrylate

The reaction in the presence of norbornene as the substitute for acrylate was also examined (Scheme 3–12). However, it resulted in a complex mixture. Similarly as the result of the experiment which was performed in Chapter 2 (Section 2.2.5, Scheme 2–14), along with benzamide **3aa** (52%), a small amount of the phenylcarbamoylation product **4** was detected as a mixture of *syn* and *anti* stereoisomers, and 2-carbamoylnorbornane **5**

was obtained in 12% yield. These carbamoylnorbornane products suggest that the reaction probably proceeds *via* a carbamoylmolybdenum intermediate. In addition, the benzoynorbornane **8** was also obtained as a mixture of *exo* and *endo* stereoisomers. Interestingly, bis(γ -lactone) derivative **9** was obtained as the mixture of two diastereomers (*syn* : *anti* = 54 : 46). The structures of the two diastereoisomers of **9** were confirmed by crystallographic X-ray analysis (Figure 3–1, 3–2).

Scheme 3–12. Attempt to trap the molybdenum intermediate by norbornene

The mechanism of the formation of the bis(γ -lactone) derivative **9** can be deduced from Iwasawa's report, which was discussed in Section 3.1, Scheme 3–6.⁴ It was proposed that the mechanism followed that reported by Iwasawa and co-workers (Scheme 3–13). Firstly, oxidative addition of phenyl iodide to complex **2a'** occurs to afford an arylmolybdenum(II) intermediate **A**. The successive insertion of a carbonyl ligand generates an acyl molybdenum complex **B**, which was inserted to norbornene to form the intermediate **C**, a second carbon monoxide insertion to offer the intermediate **D**, and

insertion of the C=O bond occurs to afford an alkyl molybdenum intermediate **E**. Finally, transmetalation and reductive elimination of intermediate **E** gives the dimeric product **9**. The formation of benzoynorbornane **8** and bis(γ -lactone) **9** indicates that the reaction involves acylmolybdenum intermediates.

Scheme 3–13. Proposed mechanism for the formation of **9**

Figure 3–1. ORTEP view for the *syn*-**9**.

Figure 3–2. ORTEP view for the *anti*-**9**.

When the reaction was performed without iodobenzene, it became rather clear and carbamoylated norbornane **5** was obtained in 30% yield (Scheme 3–14). This result indicates that the mechanism via carbamoylmolybdenum intermediate **Y** is still possible.

Scheme 3–14. Attempt to trap the molybdenum intermediate by norbornene

3.3 Conclusion

In conclusion, carbamoylation of aryl halides proceeded by using Group VI metal carbonyl amine complexes. The reaction can be applied to a large substrate scope with satisfactory yields in most cases. Furthermore, it only requires a simple experimental procedure compared to conventional palladium-catalyzed aminocarbonylation reactions. It does not require gaseous carbon monoxide and palladium catalysts.

Chapter 4 Mo(CO)₆-Mediated Carbamoylation and Alkoxy carbonylation of Aryl or Vinyl Halides

4.1 Introduction

As mentioned in section 1.3, chapter 1, the palladium-catalyzed three-component coupling reaction between aryl halides, carbon monoxide, and amines is a very powerful synthetic method to prepare amides. However, use of a large excess amount of carbon monoxide is one of the problematic points. To avoid using gaseous carbon monoxide, a variety of carbon monoxide equivalents were reported. Larhed and co-workers reported several related works on group VI metal carbonyl complexes such as Mo(CO)₆ being used as the carbon monoxide source in palladium-catalyzed three-component coupling reactions (Scheme 4–1).^{38a} Generally, these reactions have to be performed at high temperature or with microwave irradiation.

Scheme 4–1. Palladium-catalyzed three-component coupling reaction by using Mo(CO)₆ as CO source

Some metal carbonyls such as Ni(CO)₄ were reported to be used for carbonylation of aryl or alkenyl halides. For example, Bauld et al. reported Ni(CO)₄-mediated alkoxy carbonylation of aryl iodides in the presence of alcohols to afford corresponding carboxylic esters (Scheme 4–2).⁵³

Scheme 4–2. Ni(CO)₄-mediated alkoxy carbonylation of aryl iodides

In 1969, Corey and Hegedus reported the synthesis of amides or esters from reaction between aryl halides, excess amount of Ni(CO)₄, and amines or alcohols in the presence of base respectively.²² Nakayama and Mizoroki reported the stoichiometric carbonylation of aryl halides with Ni(CO)₄ in the presence of potassium acetate.⁵⁴ All these cases indicated that nickel carbonyl complex can also serve as a mediator to form carbon–carbon and carbon–nitrogen (oxygen) bonds in addition to be the source of carbon monoxide.

The carbamoylation reaction with molybdenum carbonyl amine complexes without using palladium and phosphine was described in chapter 3 (Scheme 4–3). On the other hand, Group VI metal carbonyl amine complexes can be easily prepared from amines and (CO)₅MCINEt₄ (M = Cr, Mo, W),⁴⁴ which is readily obtained by heating M(CO)₆ with Et₄NCl (Scheme 4–4). Therefore, instead of preparing molybdenum carbonyl amine complexes beforehand, it was thought to be possible to perform this carbamoylation reaction in a one-pot manner by mixing Mo(CO)₆ and amines as the source of the molybdenum carbonyl amine complexes. If group VI metal carbonyl amine complexes would be generated in situ from group VI metal carbonyl and the amine, it is possible to reduce the usage of CO in the form of M(CO)₆.

Scheme 4–3. Carbamoylation of aryl halides from molybdenum carbonyl amine complexes

Scheme 4–4. Formation of metal carbonyl amine complexes

4.2 Results and Discussion

4.2.1 Mo(CO)₆-Mediated Carbamoylation of Aryl Halides

The carbamoylation of phenyl iodide with M(CO)_6 and amine to test the possibility for one-pot way for carbamoylation of aryl halides was first examined (Table 4–1). By mixing benzylamine, iodobenzene, K_2CO_3 , NEt_4Cl and W(CO)_6 in a ratio of 1:1.2:1.1:1:1 in diglyme, after the mixture was heated at 150 °C for 12 hours, the amide **3aa** was obtained in 52% yield (entry 1). NBu_3 was found to be the best base, affording the amide **3aa** in 90% yield (entry 3). The yield of the amide was decreased to 13% in the absence of Et_4NCl (entry 4). The reaction with Mo(CO)_6 showed an efficient conversion and **3aa** was obtained in 97% yield (entry 5). Interestingly, the yield of **3aa** was not affected even when the amount of Mo(CO)_6 was decreased to 0.2 equiv. (entry 6). It is noteworthy that 0.167 equiv. of Mo(CO)_6 , which involves a stoichiometric amount of CO gave 85% yield of amide **3aa** (entry 7). These results explain the high efficiency of the catalyst to incorporate its CO ligand into the amide.

Table 4–1. Group VI metal carbonyl complex-mediated carbamoylation of phenyl iodide^a

$\text{Ph-I} + \text{Ph-CH}_2\text{NH}_2$		$\xrightarrow[\text{diglyme, 150 } ^\circ\text{C}]{\begin{array}{l} \text{M(CO)}_6 \text{ (x equiv.)} \\ \text{Et}_4\text{NCl (x equiv.)} \\ \text{base (1.1 equiv.)} \end{array}}$		$\text{Ph-C(=O)-NH-CH}_2\text{Ph}$	
1a	2a'''			3aa	
entry	M	base	x/equiv.	time/h	yield
1	W	K ₂ CO ₃	1.0	12	52
2	W	NEt ₃	1.0	12	63
3	W	NBu ₃	1.0	12	90
4 ^b	W	NBu ₃	1.0	20	13
5	Mo	NBu ₃	1.0	3	97
6	Mo	NBu ₃	0.2	3	97
7	Mo	NBu ₃	0.167	3	85

^a The reactions were carried out in the molar ratio of H₂NBn:PhI:NBu₃ = 1.0:1.2:1.1.

^b Reaction without Et₄NCl.

In order to investigate the possibility whether the reaction can be conducted in a catalytic manner, the carbamoylation was performed under a carbon monoxide atmosphere, however, it was found that the yield of the amide was dramatically decreased (Scheme 4–5). This is probably due to the fact that the carbon monoxide gas suppressing the release of CO ligand from molybdenum center, hence the oxidative addition of phenyl iodide to molybdenum was inhibited.

Scheme 4–5. Carbamoylation of iodobenzene under different atmosphere

As the carbamoylation of phenyl iodide with 0.2 equiv. of Mo(CO)₆ sufficiently proceeded, the scope of aryl halides for this reaction was next investigated (Table 4–2). Regardless of the electronic property of the substituents and substitution positions on the phenyl ring, the corresponding amides were obtained in excellent yields (entries 1–5). The naphthalenyl and heteroaromatic halides were also applicable for this reaction and the corresponding amides were obtained (entries 6–11, 14, and 15). When 1-bromo-4-iodobenzene was used, selective carbamoylation proceeded to obtain *p*-bromobenzamide **3ea** (entry 12). Interestingly, when 2-chloro-5-iodopyridine was used, *N*-benzyl-5-iodopicolinamide **3qa** was obtained as the product in 53% yield instead of the expected product, *N*-benzyl-6-chloronicotinamide (entry 11).⁵⁵ 3-Chloropyridine, in contrast, gave only a trace amount of amide despite longer reaction time (entry 13). These results suggest that the chelation-assisted oxidative addition of 2-chloropyridine to the molybdenum intermediate enhanced the reaction and gave higher yields.⁵⁶ The reaction with alkenyl halides proceeded at lower temperatures (80–100 °C), to give the corresponding α,β -unsaturated amides in good yields (entries 16–18). Although the yield was not as good, benzyl bromide was also applicable for this reaction (entry 19).

Table 4–2. Scope of aryl halides for Mo(CO)₆-mediated carbamoylation reaction^a

$ \begin{array}{c} \text{Ar-X} + \text{Ph-CH}_2\text{NH}_2 \xrightarrow[\text{diglyme, 150 } ^\circ\text{C}]{\text{Mo(CO)}_6 \text{ (0.2 equiv.)}, \text{Et}_4\text{NCl (0.2 equiv.)}, \text{NBu}_3 \text{ (1.1 equiv.)}} \text{Ar-C(=O)-NH-CH}_2\text{Ph} \\ \text{1} \qquad \qquad \text{2a'''} \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{3} \end{array} $				
entry	Ar-X	product	Time/h	yield/%
1	1a: R = H	3aa	3	97
2	1h: R = 4-OMe	3ha	4	96
3	1m: R = 3-OMe	3ma	2	99
4	1n: R = 2-OMe	3na	4	91
5	1b: R = 4-Ac	3ba	4	95
6	1d': X = 1-I	3da	1	93
7	1c: X = 2-Br	3ca	2	97
8	1i	3ia	2	94
9 ^b	1j: X ₁ = Br, X ₂ = H	3ja	0.5	45
10 ^c	1j': X ₁ = Cl, X ₂ = H	3ja	1	35
11 ^d	1q: X ₁ = Cl, X ₂ = I	3qa	2	53
12	1e	3ea	1	76
13	1r	3ra	7	trace

Continued

14 ^b	1s	3sa	0.5	61
15	1t	3ta	2	77
16 ^e 17 ^b	1o : X = Br, R = H 1u : X = Br, R = CF ₃	3oa 3ua	0.5 0.5	85 77
18 ^f	1v	3va	0.5	72
19	1k	3ka	4	52

^a The reactions were carried out with **1** (0.60 mmol), **2a'''** (0.50 mmol), and NBU₃ (0.55 mmol) in diglyme at 150 °C unless otherwise stated.

^b The reaction temperature is 90 °C. ^c The reaction temperature is 140 °C.

^d The reaction temperature is 120 °C. ^e The reaction temperature is 80 °C.

^f The reaction temperature is 100 °C.

Next, the scope of this reaction was examined with respect to the amine (Table 4–3). *N*-Arylbenzamides **3ah**, **3ai**, and **3aj** were obtained in moderate to good yields when aniline derivatives **2h–j** were used (entries 3–5). Electron-rich anilines gave a better yield indicating that the nucleophilicity of the aniline may promote the reaction. Not only aryl amines but also alkyl amines can be applied to give the corresponding amides in good yields (entries 6–9). Cyclic secondary amines such as pyrrolidine and piperidine as well as acyclic secondary amines such as methylbenzylamine and diethylamine can be used in this reaction to provide good to excellent yields (entries 10–13). Heteroaromatic amines gave the corresponding amides in good yields (entries 14–16).

Table 4–3. Scope of Amines for Mo(CO)₆-Mediated Carbamoylation Reaction^a

<div><div><div><div><div>PhI</div><div>1a</div></div><div>+</div><div><div><div>HNR¹R²</div><div>2</div></div></div></div><div><div>Mo(CO)₆ (0.2 equiv.) Et₄NCl (0.2 equiv.) NBu₃ (1.1 equiv.) diglyme, 150 °C</div><div>→</div><div><div><div>Ph-C(=O)-NR¹R²</div><div>3</div></div></div></div></div></div>				
entry	R ¹ R ² NH	product	time/h	yield/%
1	2a''' : R = H	3aa	3	97
2	2g : R = OMe	3ag	2	92
3	2h : R = H	3ah	4	79
4	2i : R = CO ₂ Me	3ai	7	64
5	2j : R = OMe	3aj	4	85
6 ^b	2e' : R = <i>n</i> -butyl	3ae	2	97
7 ^b	2k : R = <i>tert</i> -butyl	3ak	2	90
8 ^b	2l : R = cyclopropyl	3al	3	75
9 ^b	2m : R = cyclohexyl	3am	5	89
10 ^b	2f' : n = 1	3af	7	83
11 ^b	2n : n = 2	3an	6	90

Continued

	R^1R^2NH
12 ^c	2o : $R^1 = \text{Me}$, $R^2 = \text{benzyl}$	3ao	3	91
13 ^b	2p : $R^1, R^2 = \text{ethyl}$	3ap	4	53
14 ^b	2q	3aq	3	63
15	2r	3ar	6	60
16	2s	3as	6	64

^a The reactions were carried out in diglyme at 150 °C, **1a** (0.60 mmol), **2** (0.50 mmol), NBu₃ (0.55 mmol) unless otherwise mentioned.

^b The reaction was carried out with 1:5 ratio of **1a** (0.5 mmol) and **2** (2.5 mmol).

^c The reaction was carried out with 1:2 ratio of **1a** (0.5 mmol) and **2** (1.0 mmol).

The application of this Mo(CO)₆-mediated carbamoylation reaction for the lactam synthesis via intramolecular aminocarbonylation was then investigated. Primary amines **2b'** and **2c'** which contain a 2-iodoaryl moiety, were prepared and subjected to the reaction conditions to give 5- and 6- membered ring lactams **3b** and **3c** in good yields (Scheme 4–6).

Scheme 4–6. Mo(CO)₆-mediated intramolecular aminocarbonylations.

The application of this Mo(CO)₆-mediated carbamoylation to the synthesis of primary amides was also examined. To the best of our knowledge, there are no examples reported on the synthesis of primary amides by the conventional palladium-catalyzed three-component coupling reaction by means of aqueous ammonia which is the most readily available amine source.^{57,58} This is because palladium catalyst may be deactivated in the reaction conditions with aqueous ammonia.

The reaction of Mo(CO)₆-mediated carbamoylation of organic halides with aqueous ammonia was summarized in Table 4–4. When phenyl iodide was treated with aqueous ammonia in the presence of 0.2 equiv. of Mo(CO)₆, benzamide was obtained in 91% yield (entry 1). The absence of Et₄NCl did not lower the yield of the primary amide. Although the role of Et₄NCl in the reaction of primary and secondary amines was not clear, the chloride anion may coordinate to the molybdenum center and stabilize the intermediates. In the reaction with aqueous ammonia, an ammonia or water molecule may coordinate and stabilize the molybdenum intermediate instead of chloride anion. The reaction proceeded at ambient pressure, and hence, special apparatus such as a sealed tube or autoclave is not necessary. Both electron-rich and -deficient aryl iodides **1h** and **1b** afforded the corresponding primary amides **3hd** and **3bd** in moderate yields (entries 2 and 3). 3-Bromothiophene was also used in this reaction to afford amide **3id** in 54% yield (entry 4). Cinnamamide (**3od**) was obtained in good yield when β -bromostyrene (**1o**) was used (entry 5).

Table 4–4. Using aqueous ammonia to synthesize the primary amide^a

<div><div><div><div>ArX</div><div>1</div></div><div>+</div><div><div>aq. NH₃</div><div>2d'</div></div></div><div><div>Mo(CO)₆ (0.2 equiv.)</div><div>diglyme, 150 °C</div></div><div><div>Ar</div><div><div><div>O</div><div>C</div><div>NH₂</div></div><div>3</div></div></div></div>				
entry	ArX	product	time/h	yield/%
1	1a : R = H	3ad	4	91
2	1h : R = OMe	3hd	4	75
3	1b : R = Ac	3bd	1	50
4	1i	3id	4	54
5	1o	3od	1	76

^a The reactions were carried out with ArX (0.5 mmol) and aq. NH₃ (ca. 1.5 mmol, 25–28% w/w) at 150 °C.

4.2.2 Mo(CO)₆-Mediated Alkoxy carbonylation of Aryl Halides

In section 4.2.1, the Mo(CO)₆-mediated carbamoylation of aryl halides was described. Next, an expansion of the nucleophile from amines to alcohols to conduct the alkoxy carbonylation reaction was next investigated (Scheme 4–7).

Scheme 4–7. Hypothesis for the Mo(CO)₆-mediated alkoxy carbonylation of aryl halides

Firstly, the alkoxy carbonylation of 2-bromonaphthalene (**1c**) with phenol (**10a**) in the presence of base and 0.20 equiv. of Mo(CO)₆ was tested (Table 4–5). When 2-bromonaphthalene was treated with Mo(CO)₆ (0.20 equiv.), phenol (1.5 equiv.), Bu₃N (1.1 equiv.), and Et₄NCl (0.2 equiv.) in diglyme at 150 °C, phenyl naphthalene-2-carboxylate (**11ca**) was obtained in 82% yield (entry 1). The yield was not affected even in the absence of Et₄NCl (entry 2). Polar solvents such as DMF afforded lower yields (entry 3) and inorganic bases such as K₂CO₃ gave a very low yield of product (entry 4).

Table 4–5. Mo(CO)₆-mediated alkoxy carbonylation of 2-bromonaphthalene^a

entry	solvent	base	yield/%
1	diglyme	NBu ₃	82 ^b
2	diglyme	NBu ₃	82
3	DMF	NBu ₃	68
4	diglyme	K ₂ CO ₃	3

^a The reactions were carried out with **1c** (0.50 mmol), **10a** (0.75 mmol), Mo(CO)₆ (0.10 mmol) and base (0.55 mmol) in 5 ml solvent at 150 °C for 12 hours.

^b Et₄NCl (0.10 mmol) was added.

Next, the optimized reaction conditions were employed for the alkoxycarbonylation of 2-bromonaphthalene (**1c**) with different alcohols (Table 4–6). The alkoxycarbonylation reactions proceeded in good yields with mono-substituted phenols, regardless of the position and electronic property of the substituents on the phenol ring (entries 2–5). 3,5-Dimethylphenol (**10f**) gave the corresponding ester **11cf** in 75% yield (entry 6). However, 2,6-dimethylphenol (**10g**) only afforded the desired product **11cg** in 32% yield due to the steric hindrance (entry 7). Naphthalen-1-ol reacted well with 2-bromonaphthalene to give ester **10ch** in 83% yield (entry 8). Benzyl alcohol could be applied to afford benzyl naphthalene-2-carboxylate (**11ci**) in 59% yield (entry 9). This trend was also observed when alkyl alcohols were used (entries 10–13). Primary and secondary alkyl alcohols could be converted into the corresponding alkyl naphthalenecarboxylates in 48–56% yields. Due to steric hindrance, tertiary alcohols such as *tert*-butyl alcohol cannot be applied to this reaction protocol (entry 14). It is noteworthy that this molybdenum-mediated reaction is water-tolerant and naphthalene-2-carboxylic acid (**11co**) could be obtained in 45% yield in the reaction with water (entry 15).

Table 4–6. Scope of alcohols for Mo(CO)₆-mediated alkoxy carbonylation of 2-bromonaphthalene^a

entry	R-OH	product	yield (%)
1	10a: R = H	11ca	82
2	10b: R = 2-OMe	11cb	73
3	10c: R = 3-OMe	11cc	82
4	10d: R = 4-OMe	11cd	78
5	10e: R = 4-COOMe	11ce	70
6	10f	11cf	75
7	10g	11cg	32
8	10h	11ch	83
9	10i	11ci	59
10	10j	11cj	48

Continued

11	10k	11ck	51 ^b
12	10l	11cl	56 ^b
13	10m	11cm	52 ^b
14	10n	11cn	0
15	H ₂ O 10o	11co	45 ^c

^a The reactions were carried out with **1c** (0.50 mmol), **10** (0.75 mmol), Mo(CO)₆ (0.10 mmol) and NBU₃ (0.55 mmol) in 5 ml diglyme at 150 °C for 12 hours unless otherwise stated.

^b Alcohol **10** (2.50 mmol) were used.

^c H₂O (3.0 mmol) was used.

Further investigation of the scope with regard to aryl halides is summarized in Table 4–7. Both the iodobenzene and idonaphthalene can undergo alkoxycarbonylation with phenol to give esters **11ca** and **11aa** in 81 and 89% yields, respectively (entries 1 and 2). 2-, 3- and 4-Iodoanisole were converted to the corresponding esters in good yields regardless of the positions of the substitution on the benzene ring (entries 3–5). In addition to aryl iodides, aryl, heteroaryl, and vinyl bromides could be applied and the corresponding arenecarboxylate **11ga**, heteroarenecarboxylate **11ia**, and α,β -unsaturated ester **11oa** were obtained in 62–89% yields (entry 6–8). In reactions with 1-bromo-4-iodobenzene (**1e**), diphenyl terephthalate (**11ea'**) was obtained as the major product by using an excess amount of phenol (3 equiv.) (entry 10), chemoselective

alkoxycarbonylation was performed by suppressing the amount of phenol (1.1 equiv.) to afford phenyl *p*-bromobenzoate (**11ea**) as the main product in 61% yield (entry 9).

Table 4–7. Scope of aryl halides for Mo(CO)₆-mediated alkoxy carbonylation with phenol^a

$ \begin{array}{ccc} \text{Ar-X} & + & \text{Ph-OH} \\ \mathbf{1} & & \mathbf{10a} \end{array} \xrightarrow[\text{diglyme, 150 } ^\circ\text{C, 12 h}]{\text{Mo(CO)}_6 \text{ (0.2 eq.)}, \text{NBu}_3 \text{ (1.1 eq.)}} \text{Ar-CO-O-Ph} $			
entry	Ar-X	product	Yield/%
1	1c'	11ca	81

2	1a : R = H	11aa	89
3	1n : R = 2-OMe	11na	75
4	1m : R = 3-OMe	11ma	75
5	1h : R = 4-OMe	11ha	87
6	1g	11ga	62
7	1i	11ia	89

Continued

8			77
9 ^b			61 (7) ^c
10 ^d			55 (5) ^e

^a The reactions were carried out with **1** (0.50 mmol), **10a** (0.75 mmol), Mo(CO)₆ (0.10 mmol) and NBU₃ (0.55 mmol) in diglyme (5 ml) at 150 °C for 12 hours unless otherwise mentioned.

^b The reaction was carried out with a 1.1:1.0 ratio of **1e** (0.55 mmol) and **10a** (0.5 mmol).

^c The number in the parentheses is the yield of **11ea'**.

^d The molar ratio of **1e**/**10a**/Mo(CO)₆/NBU₃ = 1.0:3.0:0.4:2.2.

^e The number in the parentheses is the yield of **11ea**.

An attempt to apply the reaction for multi-acylation of di- and triols was also conducted (Table 4–8). When ethylene glycol (**10p**) and propylene glycol (**10q**) were subjected to the reactions with iodobenzene (**1a**) and Mo(CO)₆ in the molar ratio of glycol:**1a**:Mo(CO)₆ = 0.5:1.5:0.4, diacylation proceeded to give diesters **11ap** and **11aq** in 75 and 72% yields, respectively (entries 1 and 2), although the Mo(CO)₆ loading was doubled. Diacylation of hydroquinone and catechol also proceeded efficiently to afford phenylene dibenzoates **11ar** and **11as** in 81 and 70% yields, respectively (entries 3 and 4). Additionally, triacylation was performed by using triols **10t** and **10u** and triesters **11at** and **11au** were obtained in good yields (entries 5 and 6).

Table 4–8. Mo(CO)₆-mediated multi-acylation of di- or tri-ol^a

entry	R-OH	product	yield of 3
1 ^b	10p	11ap	75
2 ^b	10q	11aq	72
3	10r	11ar	81
4	10s	11as	70
5 ^c	10t	11at	72

Continued

^a The reactions were carried out with **1a** (1.50 mmol), **10** (0.50 mmol), Mo(CO)₆ (0.20 mmol) and NBu₃ (1.10 mmol) in diglyme at 150 °C for 12 hours.

^b The reactions were carried out in a molar ratio of **1a**/**10**/Mo(CO)₆/NBu₃ = 3.0:1.0:0.8:2.2.

^c The reactions were carried out in a molar ratio of **1a**/**10**/Mo(CO)₆/NBu₃ = 4.5:1.0:1.2:3.3.

Finally, intramolecular alkoxy carbonylation reactions were investigated (Scheme 4–8). When 2-iodophenyl alcohols **10v** and **10w** were treated with 0.2 equiv. of Mo(CO)₆, the corresponding five- and six-membered ring lactones **11v** and **11w** were obtained in 70 and 66% yield, respectively.

Scheme 4–8. Mo(CO)₆-mediated intramolecular alkoxy carbonylations.

4.2.3 Mechanism for the Mo(CO)₆-Mediated Carbonylation of Aryl Halides

Halides

Two possible mechanisms for this Mo(CO)₆-mediated carbonylation reaction are depicted in Scheme 4–9. One of the plausible pathways involves oxidative addition of the aryl halide and a subsequent insertion of carbon monoxide to generate acylmolybdenum intermediate **A**. Alternatively, carbamoylmolybdenum intermediate **B** could be generated by nucleophilic attack of amine or alcohol to the carbonyl ligand followed by oxidative addition of aryl halide. Although the mechanism has yet to be elucidated, it is noteworthy that molybdenum carbonyl species acts as the catalyst and most of the carbonyl ligands on the molybdenum center are incorporated into the product.

Scheme 4–9. Mechanism for the Mo(CO)₆-mediated carbonylation of aryl halides

4.3 Conclusion

In summary, an efficient Mo(CO)_6 -mediated carbonylation of aryl or vinyl halides was developed (Scheme 4–10). The procedure is simple and requires only slight excess of carbon monoxide in the form of Mo(CO)_6 . This reaction provides a method for synthesis of a variety of amides and esters from aryl halides and the amines or alcohols. The intramolecular carbonylation proceeded to produce the lactones and lactams (Scheme 4–11). Primary amides and carboxylic acids were also prepared by this methodology with aqueous ammonia and water respectively (Scheme 4–12).

Scheme 4–10. Mo(CO)_6 -mediated carbamoylation/alkoxycarbonylation of aryl halides

Scheme 4–11. Mo(CO)_6 -mediated intramolecular carbamoylation/alkoxycarbonylation

Scheme 4–12. Preparation of primary amides and carboxylic acids from aqueous ammonia and water respectively

Chapter 5 Application: Synthesis of 2-Substituted-4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-Mediated Cyclocarbonylation of *o*-Iodoanilines with Aryl or Vinyl Halides

5.1 Introduction

4*H*-3,1-Benzoxazin-4-one derivatives have been shown to possess a variety of biological properties.⁵⁹ Complexes bearing the 4*H*-3,1-benzoxazin-4-one moiety have been demonstrated to act as inhibitors of serine protease,^{59b} human leukocyte elastase (HLE).^{59h} 2-Amino-substituted 4*H*-3,1-benzoxazin-4-ones were reported to act as inhibitors of HSV-1 protease,⁵⁹ⁱ Clr serine protease,^{59e} and human cytomegalovirus protease.^{59j} Additionally, 2-substituted-4*H*-3,1-benzoxazin-4-ones have been used as the synthetic intermediates for the preparation of heterocyclic compounds such as the *N*-substituted-quinazolin-4-one derivatives (Scheme 5–1).⁶⁰

Scheme 5–1. Convert benzoxazinones to quinazolinones

There are a number of synthetic methods for the preparation of 4*H*-3,1-benzoxazin-4-ones. The most common synthetic methods include the use of anthranilic acid with 2.0 equivalent carboxylic acid chlorides to give the intermediate **B**, and an intramolecular nucleophilic displacement of benzoate ion from the anhydride group by the carbonyl oxygen of the amide group occurred to give the product **C** (Scheme 5–2).⁶¹

Similarly, 2-substituted 4*H*-3,1-benzoxazin-4-ones could be prepared from *N*-acyl anthranilic acids with acetic anhydride (Scheme 5–3).⁶²

Scheme 5–2. Preparation of benzoxazinones from anthranilic acid with carboxylic acid chlorides

Scheme 5–3. Preparation of benzoxazinones from *N*-acyl anthranilic acids with acetic anhydride

It is also reported that the 4*H*-3,1-benzoxazin-4-ones can be synthesized by palladium-catalyzed carbonylation of *o*-iodoanilines. For example, Cacchi and Marinelli reported the Pd-catalyzed synthesis of 2-aryl- and 2-vinyl-4*H*-3,1-benzoxazin-4-ones from *o*-iodoanilines and unsaturated halides or triflates (Scheme 5–4).⁶³ A proposed mechanism for this cyclocarbonylation reaction is described in Scheme 5–5. Firstly, chemoselective carbonylative insertion of palladium into the carbon–halogen bond of **A** to give the acylpalladium intermediate **B**, followed by trapping with *o*-iodoaniline to afford the *o*-iodoanilide **C**, the second carbonylative insertion affording the intermediate

D. Intramolecular nucleophilic substitution of this species produces the desired product and regenerates the palladium catalyst.

Scheme 5–4. Pd-catalyzed synthesis of 2-aryl- and 2-vinyl-4*H*-3,1-benzoxazin-4-ones from *o*-iodoanilines and aryl halides

Scheme 5–5. Mechanism of Pd-catalyzed synthesis of 2-aryl- and 2-vinyl-4*H*-3,1-benzoxazin-4-ones from *o*-iodoanilines and aryl halides

Two groups reported the synthesis of 2-substituted-4*H*-3,1-benzoxazin-4-ones by palladium-catalyzed cyclocarbonylation of *o*-iodoanilines with acid chlorides. Alper et al reported the one-pot reaction of *o*-iodoanilines with acid chlorides and carbon monoxide, in the presence of palladium acetate and diisopropylethylamine, and cyclocarbonylation occurred to afford 2-substituted-4*H*-3,1-benzoxazin-4-ones in good yields (Scheme 5–6).⁶⁴ A similar reaction mechanism was proposed to that shown in Scheme 5–5.

Scheme 5–6. 2-Substituted-4*H*-3,1-benzoxazin-4-ones formation by palladium-catalyzed cyclocarbonylation of *o*-iodoanilines with acid chlorides

Petricci et al. reported the microwave–assisted Pd/C-catalyzed cyclocarbonylation of *o*-iodoanilines with acid chlorides (Scheme 5–7).⁶⁵ 2-Iodoaniline was irradiated with different acyl chlorides, at 130 °C in the presence of CO (130 psi) Pd/C and DIPEA in DMF, the corresponding benzoxazinones were obtained.

Scheme 5–7. Microwave-assisted Pd/C-catalyzed cyclocarbonylation of *o*-iodoanilines with acid chlorides

The 2-aryl-4*H*-3,1-benzoxazin-4-ones were prepared by palladium-catalyzed self-carbonylative cyclization of *o*-iodoanilines *via* double carbon monoxide insertion (Scheme 5–8).⁶⁶ 2-Iodoaniline derivatives were used as bifunctional substrates in palladium-catalysed carbonylation.

Scheme 5–8. Palladium-catalyzed self-carbonylative cyclization of *o*-iodoanilines

Furthermore, group VI metal carbonyl complexes can be used as the catalyst for the carbamoylation of unsaturated halides (Scheme 5–9).⁶⁷ This encouraged the author to develop a new approach to synthesize the substituted 4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoanilines with aryl or vinyl halides.

Scheme 5–9. Mo(CO)₆-mediated carbamoylation of aryl halides

5.2 Results and Discussion

It was assumed that the Mo(CO)_6 -mediated cyclocarbonylation of *o*-iodoanilines with unsaturated halides would be accessible in the presence of base. Therefore, cyclocarbonylation was first carried out by using a mixture of *o*-iodoaniline (**12a**), β -bromostyrene (**1o**), Mo(CO)_6 , and a base. The results are shown in Table 5–1. Two equivalents of Mo(CO)_6 were necessary to complete the reaction to give the desired product **13oa** in 65% yield (entry 1). By using NEt_4Cl as an additive, the reaction time was shortened and the yield was increased to 82% (entry 2). The yield was reduced to 54% when the amount of β -bromostyrene was decreased to 1.5 equivalents (entry 3). *o*-Acylamidophenyl iodide **14** was obtained as the co-product in 27% yield when 1.0 equivalent of Mo(CO)_6 was used (entry 4). Compound **14** was further subjected to the same reaction conditions, which led to the desired product **13oa** in 75% yield (Scheme 5–10). This suggested that compound **14** is probably the intermediate of the cyclocarbonylation reactions.

Table 5–1. Mo(CO)_6 -mediated cyclocarbonylation of *o*-iodoanilines with β -bromostyrene^a

1o	12a			13oa	14
entry	$\text{Mo(CO)}_6/\text{equiv.}$	time/h	additives/1.0 equiv.	yield of 13oa /%	yield of 14 /%
1	2.0	20	-	65	0
2	2.0	8	NEt_4Cl	82	0
3 ^b	2.0	20	NEt_4Cl	54	0
4	1.0	20	NEt_4Cl	48	27

^a All reactions were carried out with *o*-iodoaniline **12a** (0.30 mmol), **1o** (0.90 mmol), Mo(CO)_6 (0.60 mmol), and NBu_3 (0.66 mmol) in diethylene glycol dimethyl ether (diglyme) (3.0 mL) under N_2 at 150 °C unless otherwise stated.

^b **1o** (0.45 mmol) was used.

Scheme 5–10. Mo(CO)₆-mediated carbonylative cyclization of *N*-(2-iodophenyl)cinnamamide

According to these observations, the reaction mechanism of the cyclocarbonylation was proposed as shown in Scheme 5–11. In a similar manner to the previous mechanistic study of the carbamoylation of aryl halides, there are two possible mechanisms involving acylmetal or carbamoyl metal intermediates. Here, only the mechanism involving acylmetal intermediate is described. The molybdenum complex first undergoes a chemoselective oxidative addition to the carbon–halogen bond of **1** to give the aryl molybdenum intermediate **A**. A subsequent carbon monoxide insertion into the aryl carbon–Mo bond of intermediate **A** results in acyl molybdenum intermediate **B**, which is subjected to *o*-iodoaniline in the presence of NBu₃ as base to afford intermediate **C**. Intermediate **C** then undergoes reductive elimination to generate the *o*-iodoanilide **D**, another molybdenum complex undergoes oxidative addition to the carbon–iodide bond of intermediate **D** to afford intermediate **E**, which is subjected to a second carbon monoxide insertion to yield the acylmolybdenum complex **F**. Finally, the cyclization of intermediate **F** is achieved to yield product **13** via a base-catalyzed nucleophilic substitution.

Scheme 5-11. The proposed mechanism (the alternative mechanism involving carbamoylmolybdenum intermediate is omitted.)

With the optimized reaction conditions, different substituted *o*-iodoanilines was investigated (Table 5-2). The alkyl substituted *o*-iodoanilines can be efficiently converted to the acylanthranils with excellent yields (entries 2 and 3). The *o*-iodoanilines with electron-withdrawing substituents also gave good chemical yields (entries 5-7). Functional group tolerance was also investigated by using 4-substituted iodoanilines and it was found that methoxy, nitrile, acyl groups were not affected under the reaction conditions although lower yields were obtained (entries 4, 8, 9). The structure of product **13ob** (Figure 5-1) was further confirmed by the X-ray crystallographic analysis.

Table 5–2. Mo(CO)₆-mediated cyclocarbonylation of different *o*-iodoanilines (**1**) with β -bromostyrene (**2a**)^a

entry	R	time/h	yield of 13 /%
1	H (12a)	8	82 (13oa)
2	Me (12b)	8	82 (13ob)
3	Bu ^t (12c)	6	91 (13oc)
4	OCH ₃ (12d)	6	60 (13od)
5	CF ₃ (12e)	8	63 (13oe)
6	Cl (12f)	10	69 (13of)
7	F (12g)	10	70 (13og)
8	CN (12h)	8	30 (13oh)
9	Ac (12i)	8	43 (13oi)

^aAll reactions were carried out with *o*-iodoanilines **12** (0.30 mmol), **1o** (0.90 mmol), Mo(CO)₆ (0.60 mmol), NEt₄Cl (0.30 mmol), and NBU₃ (0.66 mmol) in diethylene glycol dimethyl ether (diglyme) (3.0 mL) under N₂ at 150 °C.

Figure 5–1. ORTEP view of the compound **13ob**.

Next, the scope of this Mo(CO)_6 -mediated cyclocarbonylation reaction was investigated by using different vinyl or aryl halides (Table 5–3). The results indicate that the reaction has wide functional group compatibility for different substitutions on the phenyl ring. For instance, the alkyl, aryl, methoxy, halogen, acyl, and ethoxycarbonyl groups were compatible with the reaction conditions. Regardless of the electronic property of the substituent and substitution positions on the phenyl ring, the corresponding products were generally obtained in moderate to good yields. Comparing the reactivity of styryl halides, styryl bromides could be converted to acylanthranils in higher yield than styryl iodides (entries 1–8). This reaction system is also accessible to vinyl halides, such as the vinyl iodide substrate **1ad** as well as heterocyclic halides, such as 3-bromothiophene **1i**, providing their respective expected products in moderate yields (entries 11, 19).

Table 5–3. Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoaniline (**1a**) with different aryl or vinyl halides (**2**)^a

$ \text{Ar-X} + \text{NH}_2\text{C}_6\text{H}_4\text{I} \xrightarrow[\text{diglyme, 150 } ^\circ\text{C, 12 h}]{\text{Mo(CO)}_6 \text{ (2.0 equiv.)}, \text{NEt}_4\text{Cl (1.0 equiv.)}, \text{NBu}_3 \text{ (2.2 equiv.)}} \text{Ar-C}_6\text{H}_4\text{-N-C(=O)-O} $					
	1	12a		13	
entry	1	yield of 13 /%	entry	1	yield of 13 /%
			11		54 (13ada)
1	X = Br, 1w	80 (13wa)			
2	X = I, 1w'	67 (13wa)			
			12	R = H 1a	72 (13aa)
3	X = Br, 1x	85 (13xa)	13	R = OMe 1h	57 (13ha)
4	X = I, 1x'	68 (13xa)	14	R = Ac 1b	69 (13ba)
			15	R = Me 1ae	70 (13aea)
5	X = Br, 1y	67 (13ya)	16	R = CO ₂ Et 1g'	76 (13ga)
6	X = I, 1y'	50 (13ya)	17	R = F 1af	58 (13afa)
			18		65 (13aga)
7 ^b	X = Br, 1z	82 (13za)			
8 ^b	X = I, 1z'	65 (13za)	19		49 (13ia)
9		86 (13aba)			66 (13da)
10		55 (13aca)	20 ^c		

^a All reactions were carried out with *o*-iodoaniline **12a** (0.30 mmol), **1** (0.90 mmol), Mo(CO)₆ (0.60 mmol), NEt₄Cl (0.30 mmol), and NBu₃ (0.66 mmol) in diethylene glycol dimethyl ether (diglyme) (3.0 mL) under N₂ at 150 °C for 12 hours unless otherwise stated.

^b The reaction time is 16 hours. ^c The reaction time is 24 hours.

5.3 Conclusion

In summary, an efficient approach for preparing 2-substituted-4*H*-3,1-benzoxazin-4-one derivatives by Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoaniline with different unsaturated halides was described. The reactions proceeded efficiently to afford the desired products in moderate to good yields. The Mo(CO)₆ was used as both catalyst and carbon monoxide source in this reaction protocol. Compatibility with a wide range of functional groups, such as alkyl, aryl, methoxy, halogen, acyl, nitrile, and ethoxycarbonyl groups, made this methodology synthetically useful in organic synthesis.

Chapter 6 Experimental Section

6.1 General

^1H NMR and ^{13}C NMR spectra were recorded on 3 spectrometers, (^1H , 300 MHz; ^{13}C , 75 MHz), (^1H , 400 MHz; ^{13}C , 100 MHz), and (^1H , 500 MHz; ^{13}C , 125 MHz). Spectra were calibrated using the residual ^1H chemical shift in CDCl_3 (7.26 ppm), which were used as the internal reference standards for ^1H NMR, and CDCl_3 (77.0 ppm) for ^{13}C NMR spectra. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad. Melting points are uncorrected. Wakogel[®] B-5F (Wako Pure Chemical Industries) was used for preparative thin-layer chromatography. THF was distilled from sodium for immediately use. Toluene and dichloromethane (CH_2Cl_2) were taken from a solvent purification system. Ethanol (EtOH) was distilled from sodium and stored over MS 3A. *N,N*-Dimethylformamide (DMF) was distilled from CaH_2 and stored over MS 4Å.

6.2 Palladium-Catalyzed Carbamoylation of Aryl Halides by Tungsten Carbonyl Amine Complex

6.2.1 Synthesis of Chlorometalates 1a–1a''.

Typical Procedure:

Complexes **1a–a''** were prepared according to the literature⁴³ with modifications. A mixture of tetraethylammonium chloride (3.14 g, 18.9 mmol) and hexacarbonyltungsten (7.0 g, 19.9 mmol) in diglyme (45 ml) was stirred under N₂ atmosphere and heated at 140 °C till the mixture became a clear yellow solution. After the mixture was cooled to room temperature, hexane (40 ml) was added. After keeping the mixture at 0 °C for a short while, the formed solids were filtered, washed with hexane, dried under vacuum to obtain the product as yellow powder.

6.2.2 Synthesis of Group VI Metal Carbonyl Amine Complexes **2a–2a''**.

General procedure for preparation of group VI metal carbonyl benzylamine complexes **2a–2a''**:

Amine complexes **2a–a''** were prepared according to the literature.⁴⁴ Benzylamine was added to the suspension of (CO)₅MCINet₄ in ethanol, then the mixture was stirred overnight at room temperature. The solvent was evaporated, and the residue was purified by flash column chromatography (hexane : ethyl acetate = 20 : 1) to give the corresponding product.

benzylaminepentacarbonyltungsten (2a):⁶⁸

Yellow solid;

¹H NMR (CDCl₃, 400 MHz) δ 2.82 (br s, 2H), 3.92–3.96 (m, 2H), 7.26–7.28 (m, 2H), 7.36–7.44 (m, 3H);

¹³C NMR (CDCl₃, 100 MHz) δ 58.3, 127.4, 128.9, 129.4, 139.2, 197.9 (satellite, $J_{13\text{C}-183\text{W}}$ = 129.8 Hz), 200.7.

benzylaminepentacarbonylmolybdenum (2a'):⁶⁸

Dark yellow;

¹H NMR (CDCl₃, 400 MHz) δ 2.46 (br s, 2H), 3.81–3.85 (m, 2H), 7.24–7.26 (m, 2H), 7.35–7.43 (m, 3H);

¹³C NMR (CDCl₃, 100 MHz) δ 56.3, 127.3, 128.6, 129.3, 139.3, 204.0, 212.6.

6.2.3 Synthesis of Amine Complexes 2b and 2c**2-iodobenzylaminepentacarbonyltungsten (2b):**

2b: 48% (based on 2-iodobenzyl alcohol)

2-Iodobenzyl amine was prepared according to the literature.^{45a, 45b} **2b** was prepared according to the previous procedure. The crude product was purified by flash column chromatography (hexane : ethyl acetate = 20 : 1) to give yellow solid;

mp 120 °C (decomposed);

IR (KBr) 3311, 3263, 2069, 1961, 1938, 1915, 1884, 1849, 1587, 1465, 1359, 1205, 1163, 756, 597 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 3.01 (br s, 2H), 3.96–3.99 (m, 2H), 7.07–7.11 (m, 1H), 7.31–7.44 (m, 2H), 7.87 (d, *J* = 8 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ 62.4, 98.5, 129.4, 129.9, 130.8, 140.1, 141.7, 197.9 (satellite, *J*_{13C–183W} = 129.9 Hz), 200.8;

ESIHRMS: Found: *m/z* 233.9784. Calcd for C₇H₉NI: (M–W(CO)₅+H)⁺ 233.9780.

2-(2-iodophenyl)ethylaminepentacarbonyltungsten (**2c**):

2-(2-Iodophenyl)ethylamine was prepared according to the literature.^{45c} **2c** was prepared according to the above mentioned procedure, the crude product was purified by flash column chromatography (hexane : ethyl acetate = 20 : 1) to give yellow solid;

mp 90 °C (decomposed);

IR (KBr) 3331, 3282, 2069, 1975, 1932, 1905, 1847, 1832, 1583, 1465, 1355, 1010, 750, 596 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 2.52 (br s, 2H), 2.97 (t, *J* = 6.8 Hz, 2H), 3.09–3.16 (m, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.89 (d, *J* = 8 Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ 44.0, 53.9, 100.6, 129.1, 129.3, 129.8, 139.2, 140.2, 197.9 (satellite, $J_{13\text{C}-183\text{W}} = 130$ Hz), 200.6;
ESIHRMS: Found: m/z 247.9940. Calcd for $\text{C}_8\text{H}_{11}\text{NI}$: $(\text{M}-\text{W}(\text{CO})_5+\text{H})^+$ 247.9936.

6.2.4 Pd-Catalyzed Carbamoylation of Aryl Halide

Typical procedure for the Pd-catalyzed carbamoylation of aryl halides (Method A)

A mixture of **2a** (0.22 g, 0.50 mmol), 2-bromonaphthalene (**1c**) (0.16 g, 0.75 mmol), $\text{Pd}(\text{OAc})_2$ (0.011 g, 0.05 mmol), $\text{P}(o\text{-Tol})_3$ (0.031 g, 0.10 mmol) and K_2CO_3 (0.076 g, 0.55 mmol) in THF (5.0 ml) was refluxed for 68 hours under N_2 atmosphere, then THF was removed under the reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 8 : 1) to give *N*-benzyl-naphthalene-2-carboxamide **3ca** as a white solid (112 mg, 0.43 mmol). Yield: 86%.

Typical procedure for the Pd-catalyzed carbamoylation of aryl halides (Method B)

To a mixture of **2a** (0.22 g, 0.50 mmol), 2-bromonaphthalene (**1c**) (0.16 g, 0.75 mmol), $\text{Pd}(\text{OAc})_2$ (0.011 g, 0.05 mmol) and $\text{P}(o\text{-Tol})_3$ (0.031 g, 0.10 mmol) was added dropwise a solution of LiHMDS (0.55 ml, 0.55 mmol) in THF (5.0 mL) at -78 °C under N_2 atmosphere. After the reaction temperature was risen to room temperature, the mixture was heated to reflux for 30 hours, then THF was removed under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 8 : 1) to give *N*-benzyl-naphthalene-2-carboxamide **3ca** as a white solid (110 mg, 0.42 mmol). Yield: 84%.

***N*-benzylbenzamide (3aa):**⁶⁹

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 4.65 (d, J = 6.0 Hz, 2H), 6.42 (br s, 1H), 7.28–7.37 (m, 5H), 7.41–7.45 (dd, J = 7.6 Hz, 7.2 Hz, 2H), 7.48–7.52 (t, J = 7.2 Hz, 1H), 7.79 (d, J = 7.2 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ 44.1, 126.9, 127.6, 127.9, 128.6, 128.8, 131.5, 134.4, 138.1, 167.3.

4-acetyl-*N*-benzylbenzamide (3ba):

White solid;

mp 112–113 °C;

IR (KBr) 3292, 3091, 3066, 2918, 1685, 1639, 1606, 1552, 1421, 1361, 1323, 1300, 1263, 985, 725 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 2.60 (s, 3H), 4.63 (d, J = 5.6 Hz, 2H), 6.75 (br s, 1H), 7.28–7.35 (m, 5H), 7.86 (d, J = 8.4 Hz, 2H), 7.96 (d, J = 8.0 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 26.7, 44.2, 127.3, 127.7, 127.9, 128.5, 128.8, 137.8, 138.2, 139.1, 166.4, 197.4;

ESIHRMS: Found: m/z 254.1179. Calcd for C₁₆H₁₆NO₂: (M+H)⁺ 254.1181.

***N*-benzyl-4-(1-hydroxyethyl) benzamide (3ba'):**

Sticky liquid;

IR (CHCl₃) 3324, 2974, 2928, 1637, 1550, 1498, 1453, 1365, 1306, 1091, 1012, 898, 853, 697 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 1.49 (d, J = 4.0 Hz, 3H), 2.07 (br s, 1H), 4.64 (d, J = 8.0, 2H), 4.94 (q, J = 6.4 Hz, 1H), 6.43 (br s, 1H), 7.28–7.36 (m, 5H), 7.42 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 25.3, 44.1, 69.9, 125.5, 127.2, 127.6, 127.9, 128.8, 133.3, 138.1, 149.5, 167.1;

ESIHRMS: Found: m/z 256.1335. Calcd for C₁₆H₁₈NO₂: (M+H)⁺ 256.1338.

***N*-benzyl-naphthalene-2-carboxamide (3ca):**⁷⁰

White solid;

¹H NMR (CDCl₃, 500 MHz) δ 4.67 (d, J = 6.0 Hz, 2H), 6.90 (br s, 1H), 7.28–7.38 (m, 5H), 7.49–7.56 (m, 2H), 7.84–7.87 (m, 4H), 8.31 (s, 1H);

¹³C NMR (CDCl₃, 125 MHz) δ 44.1, 123.6, 126.6, 127.4, 127.5, 127.6, 127.7, 127.8, 128.4, 128.69, 128.8, 131.5, 132.5, 134.7, 138.2, 167.5.

***N*-benzyl-naphthalene-1-carboxamide (3da):**⁷⁰

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 4.70 (d, J = 5.6 Hz, 2H), 6.39 (br s, 1H), 7.28–7.43 (m, 6H), 7.49–7.60 (m, 3H), 7.85–7.91 (m, 2H), 8.33–8.35 (m, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ 44.1, 124.6, 124.9, 125.4, 126.4, 127.1, 127.6, 127.8, 128.3, 128.8, 130.1, 130.6, 133.6, 134.2, 138.1, 169.4.

***N*-benzyl-4-bromobenzamide (3ea):**⁷¹

White solid;

¹H NMR (CDCl₃, 300 MHz) δ 4.61 (d, J = 5.7 Hz, 2H), 6.50 (br s, 1H), 7.29–7.38 (m, 5H), 7.55 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.7 Hz, 2H);

¹³C NMR (CDCl₃, 75 MHz) δ (ppm) 44.2, 126.2, 127.7, 127.9, 128.6, 128.8, 131.8, 133.2, 137.9, 166.4.

***N*-benzyl-4-vinylbenzamide (3fa):**

White solid; mp 116–117 °C;

IR (KBr) 3280, 3261, 3082, 3030, 2922, 1641, 1564, 1502, 1454, 1427, 1357, 1323, 1246, 1078, 856, 700 cm^{-1} ;

^1H NMR (CDCl_3 , 500 MHz) δ 4.62 (d, J = 6.0 Hz, 2H), 5.35 (d, J = 11.0 Hz, 1H), 5.82 (d, J = 17.5 Hz, 1H), 6.62 (br s, 1H), 6.73 (dd, J = 11.0, 17.5 Hz, 1H), 7.27–7.35 (m, 5H), 7.43 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H);

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 44.0, 116.0, 126.2, 127.3, 127.5, 127.8, 128.7, 133.3, 135.9, 138.2, 140.6, 167.0;

ESIHRMS: Found: m/z 238.1221. Calcd for $\text{C}_{16}\text{H}_{16}\text{NO}$: ($\text{M}+\text{H}$) $^+$ 238.1232.

Ethyl 4-(benzylcarbamoyl)benzoate (3ga):⁷²

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 1.39 (t, J = 7.2 Hz, 3H), 4.37 (q, J = 7.2 Hz, 2H), 4.61 (d, J = 5.6 Hz, 2H), 6.81 (br s, 1H), 7.27–7.36 (m, 5H), 7.82 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.4 Hz, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm): 14.2, 44.2, 61.3, 127.0, 127.6, 127.9, 128.7, 129.7, 133.0, 137.9, 138.1, 165.8, 166.6.

N-benzyl-4-methoxybenzamide (3ha):⁷²

White solid;

^1H NMR (CDCl_3 , 500 MHz) δ 3.74 (s, 3H), 4.51 (d, $J = 5.5$ Hz, 2H), 6.50 (br s, 1H), 6.80 (d, $J = 8.5$ Hz, 2H), 7.18–7.27 (m, 5H), 7.68 (d, $J = 9.0$ Hz, 2H);

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 44.0, 55.3, 113.7, 126.6, 127.4, 127.8, 128.7, 128.8, 138.4, 162.1, 166.9.

***N*-benzylthiophene-3-carboxamide (3ia):**

White solid; mp 102–103 °C;

IR (KBr) 3307, 3294, 3103, 3057, 1643, 1560, 1535, 1496, 1425, 1421, 1359, 1307, 1255, 1058, 1001, 819, 746 717, 688 cm^{-1} ;

^1H NMR (CDCl_3 , 500 MHz) δ 4.57 (d, $J = 5.5$ Hz, 2H), 6.61 (br s, 1H), 7.26–7.35 (m, 6H), 7.39–7.41 (m, 1H), 7.87–7.88 (m, 1H);

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 43.7, 126.1, 126.4, 127.5, 127.8, 128.3, 128.7, 137.2, 138.2, 163.0;

ESIHRMS: Found: m/z 218.0623. Calcd for $\text{C}_{12}\text{H}_{12}\text{NOS}$: $(\text{M}+\text{H})^+$ 218.0640.

***N*-Benzyl-2-pyridinecarboxamide (3ja):**⁷³

White solid;

^1H NMR (CDCl_3 , 500 MHz) δ 4.68 (d, $J = 6.0$ Hz, 2H), 7.27–7.30 (m, 1H), 7.33–7.39 (m, 4H), 7.41–7.44 (m, 1H), 7.84–7.87 (m, 1H), 8.23–8.25 (m, 1H), 8.39 (br s, 1H), 8.52–8.53 (m, 1H);

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 43.5, 122.3, 126.2, 127.5, 127.8, 128.7, 137.4, 138.2, 148.1, 149.8, 164.2.

***N*-Benzyl-2-phenylacetamide (3ka):**⁷⁴

White solid;

^1H NMR (CDCl_3 , 500 MHz) δ 3.59 (s, 2H), 4.38 (d, J = 5.5 Hz, 2H), 5.90 (br s, 1H), 7.16 (d, J = 7.0 Hz, 2H), 7.22–7.34 (m, 8H);

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 43.5, 43.7, 127.28, 127.33, 127.4, 128.6, 128.9, 129.4, 134.8, 138.1, 170.9.

6.2.5 Pd-Catalyzed Intramolecular Carbamoylation of Aryl Halide

Typical procedure (method A)

A mixture of **2b** (0.28 g, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (6.0 mg, 0.025 mmol), $\text{P}(o\text{-Tol})_3$ (15.0 mg, 0.05 mmol) and K_2CO_3 (76.0 mg, 0.55 mmol) in THF (5.0 ml) was refluxed for 6.5 days. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 1 : 1) to give white solid (24 mg, 0.18 mmol). Yield: 36%.

Typical procedure (method B)

To the suspension of **2b** (0.28 g, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol), $\text{P}(o\text{-Tol})_3$ (15.0 mg, 0.05 mmol) was added dropwise a solution of LiHMDS (0.55 ml, 0.55 mmol) in THF (5.0 mL) at -78°C under N_2 atmosphere. After the reaction

temperature was raised to room temperature, the mixture was heated to reflux for 15 hours. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 1 : 1) to give white solid (48 mg, 0.36 mmol). Yield: 72%.

2, 3-dihydro-1*H*-isoindol-1-one (3b):⁷⁵

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 4.41 (s, 2H), 7.41–7.53 (m, 4H), 7.81 (d, J = 7.6 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 45.7, 123.2, 123.7, 128.0, 131.7, 132.1, 143.6, 172.0.

3, 4-dihydroisoquinolin-1(2*H*)-one (3c):⁷⁶

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 2.93 (t, J = 6.4 Hz, 2H), 3.49–3.53 (m, 2H), 6.65 (br s, 1H), 7.14–7.19 (m, 1H), 7.26–7.30 (m, 1H), 7.36–7.40 (m, 1H), 7.99 (d, J = 7.6 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 28.3, 40.2, 127.0, 127.2, 127.9, 128.9, 132.1, 138.8, 166.4;

ESIHRMS: Found: m/z 148.0756. Calcd for C₉H₁₀NO: (M+H)⁺ 148.0762.

6.2.6 Using Norbornene to Trap the Palladium Intermediate

A mixture of **2a** (0.22 g, 0.50 mmol), iodobenzene (**1a**) (0.16 g, 0.75 mmol), Pd(OAc)₂ (5.6 mg, 0.025 mmol), P(*o*-Tol)₃ (15.0 mg, 0.05 mmol), norbornene (71 mg, 0.75 mmol) and K₂CO₃ (138 mg, 1.0 mmol) in THF(5.0 ml) was refluxed for 20 hours under N₂ atmosphere, then THF was removed under the reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 25 : 1 to 8 : 1) to give the products.

***Rac*-(1*S*,2*S*,3*S*,4*R*)-*N*-benzyl-3-phenylbicyclo[2.2.1]heptane-2-carboxamide (*trans*-4):**

Light yellow oil;

IR (NaCl) 3304, 2954, 2872, 1643, 1546, 1494, 1298, 1238, 1217, 1029, 908, 754, 731, 698 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 1.40 (d, *J* = 10 Hz, 1H), 1.45–1.66 (m, 4H), 1.77 (d, *J* = 9.6 Hz, 1H), 2.50 (s, 2H), 2.64–2.67 (m, 1H), 3.29 (d, *J* = 6.0 Hz, 1H), 4.39 (dd, *J* = 5.6, 14.8 Hz, 1H), 4.47 (dd, *J* = 5.6, 14.4 Hz, 1H), 5.82 (br s, 1H), 7.14–7.32 (m, 10H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 23.7, 30.1, 38.8, 41.6, 42.6, 43.6, 48.3, 57.1, 125.7, 126.8, 127.3, 127.6, 128.4, 128.6, 138.6, 146.2, 173.0;

ESIHRMS: Found: *m/z* 306.1861. Calcd for C₁₆H₁₆NO₂: (M+H)⁺ 306.1858.

***Rac*-(1*S*,2*R*,3*S*,4*R*)-*N*-benzyl-3-phenylbicyclo[2.2.1]heptane-2-carboxamide (*cis*-4):**

cis-4 was obtained as an inseparable mixture with **5**.

White solid;

IR (NaCl) 3313, 3009, 2955, 2972, 1651, 1512, 1236, 1215 cm⁻¹ (a mixture with **5**);

¹H NMR (CDCl₃, 500 MHz) δ 1.24–1.28 (m, 1H), 1.33–1.37 (m, 1H), 1.42–1.47 (m, 1H), 1.61–1.70 (m, 2H), 2.45–2.48 (m, 2H), 2.62–2.64 (m, 2H), 3.07 (d, *J* = 10.0 Hz, 1H), 3.75 (dd, *J* = 5.0, 14.5 Hz, 1H), 4.00 (dd, *J* = 5.5, 14.5 Hz, 1H), 5.13 (br s, 1H), 6.80–6.83 (m, 2H), 7.17–7.28 (m, 8H);

¹³C NMR (CDCl₃, 125 MHz) δ (ppm) 28.7, 31.1, 37.5, 39.8, 42.1, 43.4, 52.9, 56.0, 126.2, 127.2, 127.9, 128.2 (overlapped), 128.4, 138.0, 142.4, 172.4;

ESIHRMS: Found: *m/z* 306.1861. Calcd for C₂₁H₂₄NO: (M+H)⁺ 306.1858.

***Rac*-(1*S*,4*R*)-*N*-Benzylbicyclo[2.2.1]heptane-2-carboxamide (**5**):⁷⁷**

Compound **5** was obtained as an inseparable mixture with *cis*-4.

White solid;

¹H NMR (CDCl₃, 500 MHz) δ 1.16–1.19 (m, 2H), 1.50–1.54 (m, 2H), 1.61–1.63 (m, 3H), 1.88–1.93 (m, 1H), 2.11–2.14 (m, 1H), 2.31 (br s, 1H), 2.41 (br s, 1H), 4.39 (dd, *J* = 5.5, 15.0 Hz, 1H), 4.44 (dd, *J* = 5.5, 14.5 Hz, 1H), 5.73 (br s, 1H), 7.32–7.35 (m, 5H);

¹³C NMR (CDCl₃, 125 MHz) δ (ppm) 28.6, 29.8, 34.4, 35.9, 36.5, 41.5, 43.6, 48.1, 127.4, 127.7, 128.7, 138.6, 175.6;

ESIHRMS: Found: *m/z* 230.1550. Calcd for C₁₅H₂₀NO: (M+H)⁺ 230.1545.

6.3 Carbamoylation of Aryl Halides by Molybdenum or Tungsten Carbonyl Amine Complexes

6.3.1 Synthesis of Group VI Metal Carbonyl Amine Complexes (2d–f)

The group VI metal carbonyl amine complexes **2d–f** were synthesized through the similar procedure which was described in section 6.2.2.

Ammoniapentacarbonyltungsten: (2d)⁵⁰

Yellow solid, 70%.

¹H NMR (DMSO-*d*₆, 400 MHz) δ 3.09 (br s, 3H);

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 198.4 (satellite, $J_{13\text{C}-183\text{W}} = 128.2$ Hz), 201.5.

Butylaminepentacarbonylmolybdenum: (2e)⁷⁸

Yellow solid, 30%.

¹H NMR (CDCl₃, 400 MHz) δ 0.95 (t, $J = 8$ Hz, 3H), 1.31–1.38 (m, 2H), 1.49–1.54 (m, 2H), 2.07 (br s, 2H), 2.70–2.76 (m, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 13.6, 19.5, 35.4, 52.2, 201.0, 204.1, 212.5.

Pyrrolidinepentacarbonylmolybdenum:(2f)⁷⁹

Yellow solid, 49%.

^1H NMR (CDCl_3 , 400 MHz) δ 1.65–1.74 (m, 2H), 1.88–1.96 (m, 2H), 2.55–2.69 (m, 3H), 3.28–3.34 (m, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 25.9, 58.5, 204.2, 212.9.

6.3.2 Carbamoylation of Aryl Halides by Molybdenum or Tungsten Carbonyl Amine Complexes

Typical procedure for the carbamoylation of aryl halides

A mixture of **2a'** (0.22 g, 0.50 mmol), iodobenzene (0.122 g, 0.6 mmol), and $n\text{Bu}_3\text{N}$ (0.101 g, 0.55 mmol) in diglyme (5.0 ml) was heated at 120 °C for 1 hour under N_2 atmosphere, then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 8 : 1) to give *N*-benzyl-naphthalene-2-carboxamide **3aa** (0.10 g, 0.475 mmol) as a white solid. Yield 95%.

N-Benzyl-3-methoxybenzamide (**3ma**):⁸⁰

Colorless oil;

^1H NMR (CDCl_3 , 400 MHz) δ 3.80 (s, 3H), 4.59 (d, J = 6.0 Hz, 2H), 6.70 (br s, 1H), 6.99–7.02 (m, 1H), 7.25–7.39 (m, 8H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 44.0, 55.3, 112.3, 117.7, 118.7, 127.5, 127.8, 128.7, 129.5, 135.8, 138.1, 159.7, 167.2.

***N*-Benzyl-2-methoxybenzamide (3na):**⁸¹

Colorless oil;

¹H NMR (CDCl₃, 400 MHz) δ 3.89 (s, 3H), 4.68 (d, J = 5.6 Hz, 2H), 6.95 (d, J = 8.4 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.25–7.37 (m, 5H), 7.41–7.46 (m, 1H), 8.21 (br s, 1H), 8.25 (dd, J = 7.6, 1.6 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 43.6, 55.8, 111.2, 121.2, 121.3, 127.1, 127.4, 128.5, 132.3, 132.7, 138.7, 157.4, 165.2.

***(E)*-N-Benzylcinnamamide (3oa):**⁸²

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 4.53 (d, J = 4.0 Hz, 2H), 6.49 (br s, 1H), 6.49 (d, J = 15.6 Hz, 1H), 7.27–7.47 (m, 10H), 7.668 (d, J = 15.6 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 43.7, 120.5, 127.4, 127.7, 127.8, 128.6, 128.7, 129.6, 134.7, 138.2, 141.2, 165.9.

***(E)*-Ethyl 4-(benzylamino)-4-oxobut-2-enoate (3pa):**⁸³

Colorless crystal;

^1H NMR (CDCl_3 , 400 MHz) δ 1.26 (t, J = 6.8 Hz, 3H), 4.12 (q, J = 7.2 Hz, 2H), 4.51 (d, J = 6.0 Hz, 2H), 6.66 (br s, 1H), 6.83 (d, J = 15.6 Hz, 1H), 6.99 (d, J = 15.6 Hz, 1H), 7.27–7.32 (m, 5H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 14.0, 43.9, 61.1, 127.7, 127.9, 128.7, 130.5, 136.3, 137.4, 163.5, 165.7.

Ethyl 4-(benzylamino)-4-oxobutanoate (3pa'):⁸⁴

Colourless oil.

^1H NMR (CDCl_3 , 400 MHz) δ 1.23 (t, J = 7.2 Hz, 3H), 2.48 (t, J = 6.8 Hz, 2H), 2.65 (t, J = 6.8 Hz, 2H), 4.09 (q, J = 7.2 Hz, 2H), 4.39 (d, J = 5.7 Hz, 2H), 6.36 (br s, 1H), 7.24–7.32 (m, 5H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 14.0, 29.5, 30.8, 43.5, 60.6, 127.3, 127.6, 128.5, 138.2, 171.3, 172.9.

Benzamide (3ad):⁸⁵

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 6.21 (br s, 2H), 7.42–7.55 (m, 3H), 7.81 (d, J = 7.6 Hz, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 127.3, 128.6, 132.0, 133.3, 169.6.

***N*-Butylbenzamide (3ae):**⁸⁶

Pale yellow oil;

¹H NMR (400MHz, CDCl₃) δ 0.89 (t, J = 8 Hz, 3H), 1.29–1.38 (m, 2H), 1.50–1.58 (m, 2H), 3.38 (dd, J = 8, 12 Hz, 2H), 6.77 (br s, 1H), 7.32–7.44 (m, 3H), 7.75 (t, J = 6 Hz, 2H);

¹³C NMR (100MHz, CDCl₃) δ 13.6, 20.0, 31.5, 39.7, 126.8, 128.2, 131.0, 134.7, 167.5.

Phenyl(pyrrolidin-1-yl)methanone (3af):⁸⁷

Colorless oil;

¹H NMR (400MHz, CDCl₃) δ 1.85–1.99 (m, 4H), 3.42 (t, J = 6.0 Hz, 2H), 3.65 (t, J = 6.0 Hz, 2H), 7.37–7.39 (m, 3H), 7.49–7.51 (m, 2H);

¹³C NMR (100MHz, CDCl₃) δ = 24.4, 26.4, 46.1, 49.6, 127.0, 128.2, 129.7, 137.2, 169.7.

6.3.3 Trapping the Molybdenum Intermediate by Acrylate

A mixture of **2a'** (0.22 g, 0.50 mmol), iodobenzene (122 mg, 0.6 mmol), methyl acrylate (430 mg, 5 mmol) and ^{*n*}Bu₃N (101 mg, 0.55 mmol) in diglyme (5 ml) was heated at 150 °C for 2 hour under N₂ atmosphere, then diglyme was removed under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl

acetate = 6 : 1) to give **3aa** (76.0 mg, 0.36 mmol, yield 72%) as a white solid along with **7** (27.0 mg, 0.14 mmol, yield 28%) as a light yellow oil.

Methyl 4-oxo-4-phenylbutanoate (**7**)⁸⁸

A light yellow oil;

¹H NMR (CDCl₃, 400 MHz) δ 2.77 (t, J = 6.4 Hz, 2H), 3.32 (t, J = 6.4 Hz, 2H), 3.70 (s, 3H), 7.46 (t, J = 7.6 Hz, 2H), 7.55–7.59 (m, 1H), 7.98 (d, J = 7.6 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 28.0, 33.4, 51.8, 128.0, 128.6, 133.2, 136.5, 173.4, 198.0.

6.3.4 Trapping the Molybdenum Intermediate by Norbornene

A mixture of **2a'** (220 mg, 0.5 mmol), iodobenzene (153 mg, 0.75 mmol), norbornene (500 mg, 5.0 mmol) and ⁿBu₃N (101 mg, 0.55 mmol) in diglyme (5.0 ml) was heated at 150 °C for 1 hour under N₂ atmosphere, then solvent was removed under

reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 25 : 1 to 6 : 1) to give the products.

The data for compound **3aa**, **4** and **5** are identical with the corresponding compound data in section 6.2.6.

Bicyclo[2.2.1]heptan-2-yl(phenyl)methanone (8**)**⁸⁹

exo:endo = 1:1

Compound **8** is a 1:1 mixture of *exo:endo* product.

Colourless oil.

¹H NMR (CDCl₃, 400 MHz) δ 1.20–1.60 (m, 14H), 1.97–2.02 (m, 2H), 2.32–2.35 (m, 2H), 2.52 (s, 1H), 2.63 (s, 1H), 3.20–3.23 (m, 1H), 3.71–3.75 (m, 1H), 7.44–7.55 (m, 6H), 7.96–7.98 (m, 4H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 24.4, 28.95, 29.0, 29.7, 30.7, 33.7, 36.2, 36.3, 37.4, 41.0, 41.1, 42.0, 49.4, 49.5, 128.3, 128.4, 128.46, 128.47, 132.57, 132.61, 136.6, 137.7, 210.4, 201.6.

Syn-9

White solid.

^1H NMR (CDCl_3 , 400 MHz) δ 0.73–0.77 (m, 4H), 1.01–1.08 (m, 2H), 1.30–1.52 (m, 6H), 2.09 (d, J = 3.6 Hz, 2H), 2.61–2.67 (m, 4H), 3.03 (d, J = 8.0 Hz, 2H), 6.35 (d, J = 8.0 Hz, 2H), 7.12–7.16 (m, 2H), 7.31–7.40 (m, 4H), 7.69 (d, J = 7.6 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 27.2, 28.4, 34.1, 39.6, 40.5, 48.1, 52.0, 95.5, 125.1, 127.7, 128.2, 132.0, 134.0, 177.5.

Anti-9

White solid.

^1H NMR (CDCl_3 , 500 MHz) δ 0.71 (m, 4H), 0.92–1.09 (m, 6H), 1.33–1.35 (m, 4H), 2.28–2.33 (m, 4H), 2.56 (d, J = 8.0 Hz, 2H), 7.39–7.45 (m, 8H), 7.75 (d, J = 7.5 Hz, 2H).

^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm) 26.9, 28.2, 34.4, 39.7, 40.1, 48.8, 51.0, 91.8, 127.4, 127.8, 128.3, 128.5, 130.7, 135.1, 178.7.

6.3.5 Trapping the Carbamoyl Molybdenum Intermediate by Norbornene

A mixture of **2a'** (220 mg, 0.5 mmol), norbornene (500 mg, 5.0 mmol) and $n\text{Bu}_3\text{N}$ (101 mg, 0.55 mmol) in diglyme (5.0 ml) was heated at 150 °C for 12 hour under N_2 atmosphere, then solvent was removed under reduced pressure and the residue was

purified by flash column chromatography (hexane : ethyl acetate = 25 : 1 to 6 : 1) to give **5** (35 mg, 0.15 mmol) as a white solid. Yield 30%.

The data for compound **5** is identical with the compound data in section 6.2.6.

6.3.6 Trapping the Molybdenum(0) Co-Product by dppe Ligand.

A mixture of **2a'** (220 mg, 0.5 mmol), iodobenzene (153 mg, 0.75 mmol), and $^n\text{Bu}_3\text{N}$ (102 mg, 0.55 mmol) in diglyme (5 ml) was heated at 150 °C for 1 hour under N_2 atmosphere. 1,2-Bis(diphenylphosphino)ethane (dppe) (198 mg, 0.5 mmol) was added after the mixture was cooled down to room temperature, then the mixture was heated for another 1 hour at 150 °C under N_2 atmosphere, then the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 20 : 1 to 10 : 1) to give **3aa** (100 mg, 0.475 mmol, yield 95%) as a white solid along with $(\text{dppe})\text{Mo}(\text{CO})_4$ (225 mg, 0.37 mmol, yield 74%) as a white solid.

(dppe)Mo(CO)₄ (6)⁹⁰

White solid;

$^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 161.94 MHz): δ 55.39.

^1H NMR (CDCl_3 , 400 MHz) δ 2.52–2.64 (m, 4H), 7.35–7.41 (m, 12H), 7.59–7.64 (m, 8H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 28.1 (AXX', $|^1J(\text{PC})+^2J(\text{PC})| = 39.5$ Hz), 128.59, 128.64, 128.7, 129.8, 131.4, 131.46, 131.53, 136.3, 136.6, 209.3 (t, $^2J(\text{PC}) = 8.7$ Hz), 217.4 (AXX', $^2J(\text{PC}) = 25.8$ Hz, $^2J(\text{PC}) = 9.2$ Hz).

6.4 $\text{Mo}(\text{CO})_6$ -Mediated Carbamoylation and Alkoxy carbonylation of Aryl or Vinyl Halides

6.4.1 $\text{Mo}(\text{CO})_6$ -Mediated Carbamoylation of Aryl Halides.

Typical procedure for the preparation of amide from amine and aryl halides

A mixture of benzyl amine (**2a'''**) (54 mg, 0.5 mmol), iodobenzene (**1a**) (123 mg, 0.6 mmol), $n\text{Bu}_3\text{N}$ (102 mg, 0.55 mmol), $\text{Mo}(\text{CO})_6$ (26 mg, 0.1 mmol) and Et_4NCl (16 mg, 0.1 mmol) in diglyme (5.0 ml) was heated at 150 °C for 3 hour under N_2 atmosphere, then the solvent was removed under the reduced pressure and the residue was purified by flash column chromatography (hexane : ethyl acetate = 20 : 1 to 8 : 1) to give *N*-benzylbenzamide **3aa** as a white solid (102 mg, 0.485 mmol). Yield: 97%.

***N*-Benzyl-5-iodopyridine-2-carboxamide (3qa):**

White solid;

mp 76–77 °C (AcOEt);

IR (NaCl, CHCl₃) 3392, 3018, 2399, 1670, 1523, 1456, 1215, 759, 669 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 4.65 (d, J = 6.0 Hz, 2H), 7.27–7.35 (m, 5H), 7.99 (d, J = 8.0 Hz, 1H), 8.17 (dd, J = 2.0, 8.0 Hz, 1H), 8.26 (br s, 1H), 8.72 (d, J = 2.0 Hz, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 43.5, 97.0, 124.0, 127.5, 127.8, 128.7, 137.9, 145.7, 148.6, 154.1, 163.7.

ESIHRMS: Found: m/z 338.9981. Calcd for C₁₃H₁₂IN₂O: (M+H)⁺ 338.9994.

***N*-Benzylquinoline-2-carboxamide (3sa):**

White solid;

mp 124–125 °C (AcOEt);

IR (NaCl, CHCl₃) 3388, 3014, 1670, 1529, 1500, 1427, 1217, 846, 771, 667 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 4.73 (d, J = 6.4 Hz, 2H), 7.24–7.40 (m, 5H), 7.57 (t, J = 7.6 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H), 8.64 (br s, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 43.5, 118.8, 127.4, 127.6, 127.77, 127.79, 128.6, 129.2, 129.5, 130.0, 137.4, 138.2, 146.4, 149.6, 164.4.

ESIHRMS: Found: m/z 263.1176. Calcd for C₁₇H₁₅N₂O: (M+H)⁺ 263.1184.

***N*-Benzyl-4,6-dimethoxy-1,3,5-triazine-2-carboxamide (3ta):**

White solid;

mp 112–114 °C (AcOEt);

IR (NaCl, CHCl₃) 3437, 3265, 3016, 2399, 1570, 1467, 1377, 1219, 1143, 1111, 819, 781, 667 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 3.89 (s, 3H), 3.95 (s, 3H), 4.64 (d, J = 6.12 Hz, 2H), 6.89 (br s, 1H), 7.25–7.32 (m, 5H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 44.7, 54.4, 54.6, 127.2, 127.5, 128.4, 138.4, 168.1, 171.9, 172.4.

ESIHRMS: Found: m/z 275.1140. Calcd for C₁₃H₁₅N₄O₃: (M+H)⁺ 275.1144.

***(E)*-N-Benzyl-3-[4-(trifluoromethyl)phenyl]acrylamide (3ua):**

White solid;

mp 163–165 °C (AcOEt);

IR (NaCl, CHCl₃) 3263, 3018, 1666, 1627, 1512, 1415, 1323, 1215, 1168, 1130, 1068, 756, 669 cm⁻¹;

¹H NMR (CDCl₃, 400 MHz) δ 4.56 (d, J = 5.8 Hz, 2H), 6.20 (br s, 1H), 6.50 (d, J = 15.6 Hz, 1H), 7.27–7.36 (m, 5H), 7.57 (dd, J = 8.4, 16.0 Hz, 4H), 7.67 (d, J = 15.6 Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 43.9, 122.9, 123.8(q, $^1J_{\text{C-F}} = 270.2$), 125.76 (q, $^3J_{\text{C-F}} = 3.7$ Hz), 127.7, 127.9 (overlapped), 128.8, 131.3 (q, $^2J_{\text{C-F}} = 32.4$ Hz), 137.9, 138.2, 139.7, 165.1.

ESIHRMS: Found: m/z 306.1110. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{OF}_3$: $(\text{M}+\text{H})^+$ 306.1106.

***N*-Benzyl-3-oxocyclopent-1-ene-1-carboxamide (3va):**

Colorless oil;

IR (NaCl , CHCl_3) 3321, 3016, 1712, 1653, 1602, 1521, 1215, 771, 667 cm^{-1} ;

^1H NMR (CDCl_3 , 400 MHz) δ 2.42–2.45 (m, 2H), 2.82–2.84 (m, 2H), 4.51 (d, $J = 5.8$ Hz, 2H), 6.46 (s, 1H), 7.03 (br s, 1H), 7.25–7.34 (m, 5H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 27.7, 35.2, 43.7, 127.7, 127.8, 128.7, 133.4, 137.3, 163.9, 168.3, 209.3.

ESIHRMS: Found: m/z 216.1025. Calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_2$: $(\text{M}+\text{H})^+$ 216.1025.

***N*-(4-Methoxybenzyl)benzamide (3ag):**⁹¹

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 3.77 (s, 3H), 4.52 (d, $J = 5.6$ Hz, 2H), 6.69 (br s, 1H), 6.85 (d, $J = 8.3$ Hz, 2H), 7.24 (d, $J = 8.3$ Hz, 2H), 7.38–7.48 (m, 3H), 7.77 (d, $J = 7.9$ Hz, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 43.5, 55.2, 114.0, 126.9, 128.4, 129.2, 130.3, 131.4, 134.4, 158.9, 167.3.

***N*-Phenylbenzamide (3ah):**⁹²

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 7.15 (t, $J = 7.6$ Hz, 1H), 7.36 (t, $J = 7.6$ Hz, 2H), 7.45–7.56 (m, 3H), 7.65 (d, $J = 7.6$ Hz, 2H), 7.86 (d, $J = 7.6$ Hz, 2H), 7.95 (br s, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 120.2, 124.5, 127.0, 128.7, 129.0, 131.8, 135.0, 137.9, 165.8.

Methyl 4-benzamidobenzoate (3ai):⁹³

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 3.92 (s, 3H), 7.49–7.60 (m, 3H), 7.75 (d, $J = 8.2$ Hz, 2H), 7.88 (d, $J = 7.2$ Hz, 2H), 7.99 (br s, 1H), 8.06 (d, $J = 8.8$ Hz, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 52.1, 119.2, 125.9, 127.1, 128.9, 130.9, 132.2, 134.5, 142.1, 165.8, 166.6.

***N*-(4-Methoxyphenyl)benzamide (3aj):**⁹⁴

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 3.82 (s, 3H), 6.91 (d, J = 9.2 Hz, 2H), 7.47–7.56 (m, 5H), 7.73 (br s, 1H), 7.86 (d, J = 7.6 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 55.5, 114.2, 122.1, 127.0, 128.7, 131.0, 131.7, 135.0, 156.6, 165.6.

***N*-tert-Butylbenzamide (3ak):**⁹⁵

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 1.46 (s, 9H), 5.99 (br s, 1H), 7.38–7.45 (m, 3H), 7.70 (d, J = 7.4 Hz, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 28.8, 51.5, 126.6, 128.4, 131.0, 135.9, 166.9.

***N*-Cyclopropylbenzamide (3al):**⁹⁶

White solid;

¹H NMR (CDCl₃, 400 MHz) δ 0.59–0.63 (m, 2H), 0.81–0.86 (m, 2H), 2.85–2.91 (m, 1H), 6.49 (br s, 1H), 7.36–7.48 (m, 3H), 7.73 (d, J = 7.6 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 6.6, 23.1, 126.8, 128.4, 131.3, 134.3, 168.9.

***N*-Cyclohexylbenzamide (3am):**⁹⁷

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 1.10–1.43 (m, 5H), 1.59–1.75 (m, 3H), 1.97–2.00 (m, 2H), 3.89–3.98 (m, 1H), 6.23 (br s, 1H), 7.35–7.46 (m, 3H), 7.74 (d, $J = 7.2$ Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 24.9, 25.4, 33.1, 48.6, 126.8, 128.3, 131.1, 135.0, 166.6.

1-Benzoylpiperidine (3an):⁹⁸

Colorless oil;

^1H NMR (CDCl_3 , 400 MHz) δ 1.48 (br s, 2H), 1.65 (br s, 4H), 3.31 (br s, 2H), 3.68 (br s, 2H), 7.36 (br s, 5H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 24.5, 25.5, 26.4, 43.0, 48.7, 126.7, 128.3, 129.2, 136.4, 170.2.

***N*-Benzyl-*N*-methylbenzamide (3ao):**⁹⁹

Colorless oil;

¹H NMR (CDCl₃, 400 MHz) δ 2.86 (br s, 1.5H), 3.03 (br s, 1.5H), 4.51 (br s, 1H), 4.76 (br s, 1H), 7.17–7.47 (m, 10H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 33.1, 36.9, 50.7, 55.1, 126.7, 126.9, 127.4, 128.1, 128.4, 128.6, 128.7, 129.5, 136.2, 136.5, 136.9, 171.5, 172.2.

***N,N*-diethylbenzamide (3ap):**¹⁰⁰

Colorless oil;

¹H NMR (CDCl₃, 400 MHz) δ 1.09 (br s, 3H), 1.23 (br s, 3H), 3.23 (br s, 2H), 3.53 (br s, 2H), 7.36 (br s, 5H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 12.8, 14.2, 39.2, 43.2, 126.2, 128.3, 129.0, 137.2, 171.3.

1-Benzoyl-1*H*-pyrrole (3aq):¹⁰¹

Colorless oil,

^1H NMR (CDCl_3 , 400 MHz) δ 6.35 (m, 2H), 7.29 (m, 2H), 7.49–7.63 (m, 3H), 7.75 (d, J = 7.6 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 113.1, 121.3, 128.5, 129.5, 132.3, 133.2, 167.7.

***N*-Benzoyl-1*H*-indole (3ar):**¹⁰²

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 6.62 (d, J = 7.6 Hz, 1H), 7.29–7.39 (m, 3H), 7.41–7.62 (m, 4H), 7.74 (d, J = 7.6 Hz, 2H), 8.40 (d, J = 8.4 Hz, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 108.5, 116.4, 120.9, 123.9, 124.9, 127.6, 128.6, 129.2, 130.8, 131.9, 134.6, 136.0, 168.7.

***N*-Benzoyl-9*H*-carbazole (3as):**¹⁰³

White solid;

^1H NMR (CDCl_3 , 400 MHz) δ 7.32–7.38 (m, 4H), 7.52–7.55 (m, 4H), 7.66 (t, J = 7.2 Hz, 1H), 7.74 (d, J = 7.6 Hz, 2H), 8.02 (d, J = 8.0 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 115.7, 119.8, 123.4, 126.0, 126.7, 128.9, 129.0, 132.3, 135.7, 139.1, 169.6.

4-Methoxybenzamide (3hd):¹⁰⁴

White solid;

¹H NMR (DMSO-*d*₆, 400MHz): δ 3.79 (s, 3H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.86 (d, *J* = 8.8 Hz, 2H).

¹³C NMR (DMSO-*d*₆, 100MHz): δ (ppm) 55.3, 113.4, 126.5, 129.4, 161.6, 167.5.

4-Acetylbenzamide (3bd):^{51f}

White solid;

¹H NMR (DMSO-*d*₆, 400MHz): δ 2.61 (s, 3H), 7.57 (br s, 1H), 8.00 (s, 4H), 8.18 (br s, 1H).

¹³C NMR (DMSO-*d*₆, 100MHz): δ (ppm) 27.0, 127.8, 128.1, 138.1, 138.7, 167.2, 197.8.

Thiophene-3-carboxamide (3id):¹⁰⁵

White solid;

¹H NMR (DMSO-*d*₆, 400MHz): δ 7.25 (br s, 1H), 7.48–7.56 (m, 2H), 7.79 (br s, 1H), 8.13 (d, *J* = 1.6 Hz, 1H).

^{13}C NMR (DMSO- d_6 , 100MHz): δ (ppm) 126.6, 127.2, 129.1, 138.0, 163.8.

Cinnamamide (3od):¹⁰⁶

White solid;

^1H NMR (CDCl_3 , 400MHz): δ 5.65 (br s, 2H), 6.46 (d, J = 15.6 Hz, 1H), 7.37–7.38 (m, 3H), 7.51–7.53 (m, 2H), 7.65 (d, J = 15.6 Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 119.5, 127.9, 128.8, 130.0, 134.5, 142.5, 167.9.

6.4.2 Synthesis of 2b' and 2c'.

Compounds **2b'**⁴ and **2c'**⁵ were known compounds and prepared according to the literatures.

Light yellow oil;

^1H NMR (CDCl_3 , 400MHz): δ 1.79 (br s, 2H), 3.84 (s, 2H), 6.92–6.96 (m, 1H), 7.29–7.36 (m, 2H), 7.80 (d, J = 7.96 Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 51.2, 98.9, 128.3, 128.45, 128.5, 139.3, 144.9.

Light yellow oil;

^1H NMR (CDCl_3 , 400MHz): δ 1.64 (br s, 2H), 2.84–2.95 (m, 4H), 6.86–6.91 (m, 1H), 7.19–7.30 (m, 2H), 7.80 (d, $J = 7.88$ Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 42.3, 44.6, 100.9, 128.1, 128.3, 130.0, 139.6, 142.3.

6.5 $\text{Mo}(\text{CO})_6$ -Mediated Alkoxycarbonylation of Aryl Halides

6.5.1 Synthesis of 2-(2-Iodophenyl)ethanol (**10w**) and 1,1,1-tris(hydroxymethyl) phenylmethane (**10u**)

2-(2-Iodophenyl)ethanol (**10w**) was synthesized from 2-(2-bromophenyl)ethanol as a colourless oil according to the reported procedure.¹⁰⁷

Colourless oil;

^1H NMR (CDCl_3 , 400MHz): δ 1.96 (br s, 1H), 2.99 (t, $J = 6.8$ Hz, 2H), 3.82 (t, $J = 6.8$ Hz, 2H), 6.88–6.92 (m, 1H), 7.23–7.29 (m, 2H), 7.82 (d, $J = 7.6$ Hz, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 43.6, 62.1, 100.7, 128.2, 128.3, 130.3, 139.6, 141.0.

The 1,1,1-tris(hydroxymethyl)phenylmethane (**10u**) was synthesized from phenylacetaldehyde as a white solid according to the reported procedure.¹⁰⁸

¹H NMR (CDCl₃, 400MHz): δ 2.46 (br s, 3H), 4.09 (s, 6H), 7.27–7.39 (m, 5H);

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 48.9, 66.9, 126.8, 127.2, 129.0, 139.4.

6.5.2 General Procedure for Mo(CO)₆-Mediated Alkoxycarbonylation of Aryl Halides

A mixture of alcohol (**10**) (0.75 mmol), aryl halide (**1**) (0.50 mmol), Mo(CO)₆ (0.0264 g, 0.10 mmol) and NBU₃ (0.102 g, 0.55 mmol) in diglyme (5 mL) was heated at 150 °C for 12 hour under N₂ atmosphere. The solvent was removed under reduced pressure after the reaction was completed and the residue was purified by flash column chromatography (SiO₂, hexane:ethyl acetate = 19:1) to afford the ester product (**11**).

Phenyl naphthalene-2-carboxylate (**11ca**).¹⁰⁹

White solid.

¹H NMR (CDCl₃, 300 MHz) δ 7.30–7.35 (m, 3H), 7.46–7.52 (m, 2H), 7.57–7.68 (m, 2H),

7.92–8.04 (m, 3H), 8.24 (dd, J = 1.5, 8.4 Hz, 1H), 8.83 (s, 1H).

^{13}C NMR (CDCl_3 , 75 MHz) δ 121.7, 125.4, 125.9, 126.7, 126.8, 127.8, 128.3, 128.6, 129.4, 129.5, 131.9, 132.4, 135.8, 151.0, 165.3.

2-Methoxyphenyl naphthalene-2-carboxylate (11cb).

White solid; mp 89–91 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3053, 1734, 1500, 1284, 1265, 1192, 736, 704 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz) δ 3.85 (s, 3H), 7.02–7.08 (m, 2H), 7.24–7.33 (m, 2H), 7.56–7.67 (m, 2H), 7.92–8.03 (m, 3H), 8.27 (dd, J = 1.5, 8.5 Hz, 1H), 8.87 (s, 1H).

^{13}C NMR (CDCl_3 , 75 MHz) δ 55.8, 112.5, 120.8, 122.9, 125.6, 126.6, 126.7, 126.9, 127.7, 128.2, 128.4, 129.4, 131.9, 132.4, 135.7, 140.0, 151.3, 164.8.

ESIHRMS: Found: m/z 279.1025. Calcd for $\text{C}_{18}\text{H}_{15}\text{O}_3$: $(\text{M}+\text{H})^+$ 279.1021.

3-Methoxyphenyl naphthalene-2-carboxylate (11cc).

White solid; mp 72–74 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3059, 1730, 1629, 1608, 1489, 1265, 1220, 1190, 1138, 1062, 954, 775 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz) δ 3.84 (s, 3H), 6.86–6.93 (m, 3H), 7.35–7.40 (m, 1H), 7.56–7.67 (m, 2H), 7.91–8.02 (m, 3H), 8.22 (dd, J = 1.8, 8.7 Hz, 1H), 8.81 (s, 1H).

^{13}C NMR (CDCl_3 , 75 MHz) δ 55.3, 107.7, 111.8, 113.9, 125.4, 126.7, 126.8, 127.8, 128.3, 128.5, 129.4, 129.8, 131.8, 132.4, 135.7, 152.0, 160.5, 165.2.

ESIHRMS: Found: m/z 279.1026. Calcd for $\text{C}_{18}\text{H}_{15}\text{O}_3$: $(\text{M}+\text{H})^+$ 279.1021.

4-Methoxyphenyl naphthalene-2-carboxylate (11cd).

White solid; mp 122–124 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3057, 1730, 1629, 1506, 1265, 1193, 1128, 1078, 1066, 736 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz) δ 3.86 (s, 3H), 6.98–7.02 (d, J = 9.0 Hz, 2H), 7.20–7.25 (m, 2H), 7.58–7.69 (m, 2H), 7.93–8.04 (m, 3H), 8.23 (dd, J = 1.8, 8.6 Hz, 1H), 8.82 (s, 1H).

^{13}C NMR (CDCl_3 , 75 MHz) δ 55.6, 114.5, 122.5, 125.4, 126.75, 126.80, 127.8, 128.3, 128.5, 129.4, 131.8, 132.5, 135.7, 144.5, 157.3, 165.7.

ESIHRMS: Found: m/z 279.1022. Calcd for $\text{C}_{18}\text{H}_{15}\text{O}_3$: $(\text{M}+\text{H})^+$ 279.1021.

4-(Methoxycarbonyl)phenyl naphthalene-2-carboxylate (11ce).

White solid; mp 149–151 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3055, 1745, 1720, 1265, 1190, 893, 736, 704 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz) δ 3.94 (s, 3H), 7.36 (d, J = 8.7 Hz, 2H), 7.55–7.67 (m, 2H), 7.90–8.00 (m, 3H), 8.14–8.20 (m, 3H), 8.79 (s, 1H).

^{13}C NMR (CDCl_3 , 75 MHz) δ 52.1, 121.7, 125.3, 126.2, 126.9, 127.7, 127.8, 128.4, 128.7, 129.4, 131.2, 132.0, 132.4, 135.8, 154.6, 164.7, 166.3.

ESIHRMS: Found: m/z 307.0972. Calcd for $\text{C}_{19}\text{H}_{15}\text{O}_4$: $(\text{M}+\text{H})^+$ 307.0970.

3,5-Dimethylphenyl naphthalene-2-carboxylate (11cf).

White solid; mp 68–70 °C (AcOEt);

IR (NaCl, CH_2Cl_2) 3055, 1730, 1618, 1591, 1265, 1220, 1192, 1138, 1072, 738, 704 cm^{-1} ;

^1H NMR (CDCl_3 , 300 MHz) δ 2.39 (s, 6H), 6.93–6.95 (m, 3H), 7.57–7.67 (m, 2H), 7.92–8.03 (m, 3H), 8.22 (d, J = 8.4 Hz, 1H), 8.81 (s, 1H);

^{13}C NMR (CDCl_3 , 75 MHz) δ 21.2, 119.3, 125.4, 126.7, 126.9, 127.6, 127.8, 128.3, 128.5, 129.4, 131.8, 132.5, 135.7, 139.3, 150.9, 165.5.

ESIHRMS: Found: m/z 277.1232. Calcd for $\text{C}_{19}\text{H}_{17}\text{O}_2$: $(\text{M}+\text{H})^+$ 277.1229.

2,6-Dimethylphenyl naphthalene-2-carboxylate (11cg).

White solid; mp 102–104 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3057, 1728, 1629, 1469, 1354, 1265, 1224, 1192, 1168, 1128, 1091, 1064, 950, 866, 827, 775, 736 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz) δ 2.25 (s, 6H), 7.12–7.17 (m, 3H), 7.58–7.68 (m, 2H), 7.94–8.04 (m, 3H), 8.26 (dd, J = 1.6, 8.4 Hz, 1H), 8.86 (s, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 16.4, 125.5, 125.9, 126.5, 126.8, 127.8, 128.4, 128.6, 128.62, 129.5, 130.4, 131.9, 132.5, 135.8, 148.4, 164.5.

ESIHRMS: Found: m/z 277.1237. Calcd for $\text{C}_{19}\text{H}_{17}\text{O}_2$: $(\text{M}+\text{H})^+$ 277.1229.

Naphthalen-1-yl naphthalene-2-carboxylate (11ch).

Light yellow solid; mp 117–119 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3053, 1735, 1265, 1220, 1190, 1089, 740, 704 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz) δ 7.45 (d, J = 7.2 Hz, 1H), 7.50–7.70 (m, 5H), 7.83 (d, J = 8.0 Hz, 1H), 7.93–8.07 (m, 5H), 8.34 (dd, J = 1.6, 8.4 Hz, 1H), 8.96 (s, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 118.3, 121.3, 125.48, 125.51, 126.1, 126.5, 126.9, 127.0, 127.9, 128.1, 128.5, 128.7, 129.5, 132.1, 132.5, 134.7, 135.9, 146.9, 165.4.

ESIHRMS: Found: m/z 299.1078. Calcd for $\text{C}_{21}\text{H}_{15}\text{O}_2$: $(\text{M}+\text{H})^+$ 299.1072.

Benzyl naphthalene-2-carboxylate (11ci).¹¹⁰

White solid.

^1H NMR (CDCl_3 , 400 MHz) δ 5.47 (s, 2H), 7.37–7.62 (m, 7H), 7.89 (d, J = 8.8 Hz, 2H), 7.96 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.68 (s, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 66.8, 125.2, 126.6, 127.3, 127.7, 128.1, 128.2, 128.22, 128.6, 129.3, 131.2, 132.4, 135.5, 136.1, 166.5.

2-(4-Methoxyphenyl)ethyl naphthalene-2-carboxylate (11cj).

White solid; mp 95–97 °C (AcOEt).

IR (NaCl, CH₂Cl₂) 3055, 1714, 1631, 1514, 1265, 1228, 1195, 1130, 1095, 736, 704 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 3.06 (t, J = 7.2 Hz, 2H), 3.77 (s, 3H), 4.54 (t, J = 7.2 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.50–7.58 (m, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 8.57 (s, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 34.4, 55.2, 65.8, 113.9, 125.2, 126.6, 127.5, 127.7, 128.1, 128.2, 129.3, 129.85, 129.91, 131.0, 132.4, 135.5, 158.3, 166.6.

ESIHRMS: Found: m/z 307.1337. Calcd for C₂₀H₁₉O₃: (M+H)⁺ 307.1334.

2-Methylpropyl naphthalene-2-carboxylate (11ck).

Colourless oil.

IR (NaCl, CH₂Cl₂) 3059, 2962, 1712, 1631, 1469, 1375, 1276, 1226, 1195, 1130, 1095, 989, 866, 825, 779, 761 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz) δ 1.09 (d, J = 6.6 Hz, 6H), 2.17 (hept, J = 6.6 Hz, 1H), 4.20 (d, J = 6.6 Hz, 2H), 7.54–7.64 (m, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 7.8 Hz, 1H), 8.10 (dd, J = 1.5, 8.6 Hz, 1H), 8.64 (s, 1H).

¹³C NMR (CDCl₃, 75 MHz) δ (ppm) 19.2, 28.0, 71.1, 125.2, 126.6, 127.7, 127.8, 128.08, 128.13, 129.3, 130.9, 132.5, 135.5, 166.8.

ESIHRMS: Found: m/z 229.1235. Calcd for C₁₅H₁₇O₂: (M+H)⁺ 229.1229.

Pentyl naphthalene-2-carboxylate (11cl).¹¹¹

Colourless oil.

IR (NaCl, CH₂Cl₂) 3059, 2956, 2870, 1712, 1631, 1467, 1354, 1278, 1228, 1195, 1130, 1095, 970, 866, 779, 738, 704 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz) δ 0.97 (t, J = 7.2 Hz, 3H), 1.40–1.51 (m, 4H), 1.77–1.88 (m, 2H), 4.40 (t, J = 6.6 Hz, 2H), 7.51–7.61 (m, 2H), 7.87 (d, J = 8.7 Hz, 2H), 7.96 (d, J = 8.1 Hz, 1H), 8.10 (dd, J = 1.5, 8.6 Hz, 1H), 8.63 (s, 1H).

¹³C NMR (CDCl₃, 75 MHz) δ (ppm) 13.9, 22.3, 28.2, 28.4, 65.2, 125.2, 126.5, 127.67, 127.73, 128.0, 128.1, 129.3, 130.9, 132.5, 135.4, 166.8.

ESIHRMS: Found: m/z 243.1387. Calcd for C₁₆H₁₉O₂: (M+H)⁺ 243.1385.

Cyclopentyl naphthalene-2-carboxylate (11cm).

Colourless oil.

IR (NaCl, CH₂Cl₂) 3059, 2964, 2827, 1708, 1631, 1465, 1352, 1284, 1228, 1197, 1130, 1097, 962, 866, 779, 761, 736, 704 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 1.64–2.06 (m, 8H), 5.46–5.49 (m, 1H), 7.52–7.60 (m, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.96 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 8.57 (s, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 23.9, 32.8, 77.8, 125.3, 126.5, 127.7, 128.0, 128.07, 128.13, 129.3, 130.8, 132.5, 135.4, 166.5.

ESIHRMS: Found: m/z 241.1229. Calcd for C₁₆H₁₇O₂: (M+H)⁺ 241.1229.

Naphthalene-2-carboxylic acid (11co).¹¹²

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 7.56–7.65 (m, 2H), 7.92 (m, 2H), 8.00 (d, J = 8.4 Hz, 1H), 8.14 (dd, J = 1.6, 8.4 Hz, 1H), 8.74 (s, 1H).

¹³C NMR (CDCl₃, 75 MHz) δ (ppm) 125.4, 126.5, 126.8, 127.8, 128.3, 128.7, 129.5, 132.2, 132.4, 135.9, 172.2.

Phenyl naphthalene-1-carboxylate (11ca).¹¹³

White solid.

¹H NMR (CDCl₃, 300 MHz) δ 7.35–7.73 (m, 8H), 7.96 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.1 Hz, 1H), 8.53 (dd, J = 1.2, 7.5 Hz, 1H), 9.13 (d, J = 8.7 Hz, 1H).

¹³C NMR (CDCl₃, 75 MHz) δ (ppm) 121.8, 124.4, 125.7, 125.8, 125.9, 126.3, 128.1, 128.6, 129.5, 131.1, 131.6, 133.8, 134.2, 150.9, 165.7.

Phenyl benzoate (11aa).⁶⁵

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 7.20–7.27 (m, 3H), 7.42 (t, J = 8.0 Hz, 2H), 7.49 (t, J = 8.0 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 8.20 (d, J = 7.6 Hz, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 121.7, 125.8, 128.5, 129.4, 129.5, 130.1, 133.5, 150.9, 165.1.

Phenyl 2-methoxybenzoate (11na).¹¹⁴

Pale yellow solid.

¹H NMR (CDCl₃, 400 MHz) δ 3.91 (s, 1H), 7.00–7.05 (m, 2H), 7.20–7.25 (m, 3H), 7.38–7.54 (m, 3H), 8.01 (d, J = 7.6 Hz, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 55.9, 112.1, 119.0, 120.1, 121.8, 125.6, 129.3, 132.1, 134.2, 150.9, 159.8, 164.3.

Phenyl 3-methoxybenzoate (11ma).¹¹⁵

White solid.

^1H NMR (CDCl_3 , 400 MHz) δ 3.85 (s, 3H), 7.15–7.28 (m, 4H), 7.41 (q, $J = 8.0$ Hz, 3H), 7.70 (m, 1H), 7.80 (d, $J = 8.0$ Hz, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 55.4, 114.4, 120.1, 121.6, 122.5, 125.8, 129.4, 129.5, 130.8, 150.9, 159.6, 165.0.

Phenyl 4-methoxybenzoate (11ha).¹¹⁵

White solid.

^1H NMR (CDCl_3 , 400 MHz) δ 3.86 (s, 3H), 6.96 (d, $J = 9.2$ Hz, 2H), 7.19–7.26 (m, 3H), 7.41 (t, $J = 8.0$ Hz, 2H), 8.14 (d, $J = 9.2$ Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 55.4, 113.8, 121.7, 121.8, 125.6, 129.4, 132.2, 151.0, 163.8, 164.8.

Ethyl phenyl terephthalate (11ga).

White solid; mp 99–101 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3055, 1737, 1716, 1635, 1490, 1408, 1265, 1195, 1107, 1076, 1018, 736, 705 cm^{-1} .

^1H NMR (CDCl_3 , 300 MHz) δ 1.45 (t, $J = 7.2$ Hz, 3H), 4.45 (q, $J = 7.2$ Hz, 2H), 7.24–7.33 (m, 3H), 7.46 (t, $J = 7.8$ Hz, 2H), 8.19 (d, $J = 8.4$ Hz, 2H), 8.28 (d, $J = 8.4$ Hz, 2H).

^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm) 14.2, 61.5, 121.5, 126.0, 129.5, 129.6, 130.0, 133.2, 134.8, 150.7, 164.3, 165.6.

ESIHRMS: Found: m/z 271.0974. Calcd for $\text{C}_{16}\text{H}_{15}\text{O}_4$: $(\text{M}+\text{H})^+$ 271.0970.

Phenyl thiophene-3-carboxylate (11ia).¹¹⁶

White solid; mp 59–61 °C (AcOEt).

IR (NaCl, CH_2Cl_2) 3113, 1728, 1643, 1595, 1521, 1492, 1417, 1400, 1246, 1195, 1163, 1082, 1068, 931, 873, 842, 734, 688 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz) δ 7.19–7.25 (m, 3H), 7.34–7.43 (m, 3H), 7.65 (dd, $J = 1.2$, 5.2 Hz, 1H), 8.29 (dd, $J = 1.2$, 3.2 Hz, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 121.6, 125.8, 126.3, 128.2, 129.4, 132.8, 134.0, 150.6, 161.0.

ESIHRMS: Found: m/z 205.0324. Calcd for $\text{C}_{11}\text{H}_9\text{O}_2\text{S}$: $(\text{M}+\text{H})^+$ 205.0323.

Phenyl cinnamate (11oa).¹¹⁷

Pale yellow solid.

^1H NMR (CDCl_3 , 400 MHz) δ 6.03 (d, $J = 16.0$ Hz, 1H), 7.16–7.25 (m, 3H), 7.31–7.47 (m, 5H), 7.54–7.58 (m, 2H), 7.87 (d, $J = 16.0$ Hz, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 117.2, 121.6, 125.7, 128.2, 128.9, 129.4, 130.6, 134.1, 146.5, 150.7, 165.3.

Phenyl 4-bromobenzoate (11ea).¹¹⁸

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 7.19–7.29 (m, 3H), 7.26 (m, 1H), 7.40–7.44 (m, 2H), 7.64 (d, J = 8.4 Hz, 2H), 8.05 (d, J = 8.4 Hz, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 121.6, 126.0, 128.5, 128.8, 129.5, 131.6, 131.9, 150.7, 164.4.

Diphenyl terephthalate (11ea').¹¹⁹

White solid; mp 192–194 °C (AcOEt).

IR (NaCl, CH₂Cl₂) 3057, 1732, 1454, 1265, 1192, 1078, 916, 871, 848, 740, 719 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 7.24–7.33 (m, 6H), 7.46 (t, J = 8.0 Hz, 4H), 8.34 (s, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 121.6, 126.2, 129.6, 130.3, 133.9, 150.8, 164.4.

ESIHRMS: Found: m/z 319.0976. Calcd for C₂₀H₁₅O₄: (M+H)⁺ 319.0970.

Ethylene dibenzoate (11ap).¹²⁰

White solid.

^1H NMR (CDCl_3 , 400 MHz) δ 4.67 (s, 4H), 7.44 (t, $J = 8.0$ Hz, 4H), 7.56 (t, $J = 8.0$ Hz, 2H), 8.07 (d, $J = 8.0$ Hz, 4H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 62.7, 128.4, 129.7, 129.8, 133.1, 166.3.

ESIHRMS: Found: m/z 271.0969. Calcd for $\text{C}_{16}\text{H}_{15}\text{O}_4$: $(\text{M}+\text{H})^+$ 271.0970.

1,3-Propylene dibenzoate (11aq).¹²¹

Colorless oil.

IR (NaCl , CH_2Cl_2) 1728, 1452, 1288, 1109, 1070, 715 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz) δ 2.27 (quin, $J = 8.0$ Hz, 2H), 4.51 (t, $J = 8.0$ Hz, 4H), 7.42 (t, $J = 8.0$ Hz, 4H), 7.55 (t, $J = 8.0$ Hz, 2H), 8.04 (d, $J = 8.0$ Hz, 4H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 28.2, 61.7, 128.3, 129.5, 130.0, 133.0, 166.5.

ESIHRMS: Found: m/z 285.1125. Calcd for $\text{C}_{17}\text{H}_{17}\text{O}_4$: $(\text{M}+\text{H})^+$ 285.1127.

***p*-Phenylene dibenzoate (11ar).**¹²²

White crystal.

^1H NMR (CDCl_3 , 400 MHz) δ 7.30 (s, 4H), 7.53 (t, $J = 8.0$ Hz, 4H), 7.66 (t, $J = 8.0$ Hz, 2H), 8.21 (d, $J = 8.0$ Hz, 4H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 122.6, 128.6, 129.4, 130.2, 133.7, 148.4, 165.0.

ESIHRMS: Found: m/z 319.0971. Calcd for $\text{C}_{20}\text{H}_{15}\text{O}_4$: $(\text{M}+\text{H})^+$ 319.0970.

***o*-Phenylene dibenzoate (11as).**¹²²

Colorless oil.

¹H NMR (CDCl₃, 400 MHz) δ 7.32–7.40 (m, 8H), 7.52 (t, J = 8.0 Hz, 2H), 8.06 (d, J = 8.0 Hz, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 123.5, 126.7, 128.4, 128.7, 130.1, 133.6, 142.5, 164.2.

ESIHRMS: Found: m/z 319.0967. Calcd for C₂₀H₁₅O₄: (M+H)⁺ 319.0970.

3-(Benzoyloxy)-2-[(benzoyloxy)methyl]-2-methylpropyl benzoate (11at).¹²³

Colorless oil.

IR (NaCl, CH₂Cl₂) 1714, 1600, 1450, 1381, 1265, 1176, 1109, 1026, 707 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 1.32 (s, 3H), 4.50 (s, 6H), 7.42 (t, J = 8.0 Hz, 6H), 7.56 (t, J = 8.0 Hz, 3H), 8.03 (d, J = 8.0 Hz, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 17.5, 39.2, 66.6, 128.4, 128.56, 128.65, 133.1, 166.2.

ESIHRMS: Found: m/z 433.1656. Calcd for C₂₆H₂₅O₆: (M+H)⁺ 433.1651.

3-(Benzoyloxy)-2-[(benzoyloxy)methyl]-2-phenylpropyl benzoate (11au).¹²⁴

Colorless oil.

IR (NaCl, CH₂Cl₂) 1718, 1600, 1450, 1265, 1176, 1111, 1026, 709 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 4.95 (s, 6H), 7.31–7.59 (m, 14H), 7.94 (d, *J* = 8.0 Hz, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 46.2, 65.8, 126.5, 127.6, 128.4, 128.9, 129.48, 129.53, 133.1, 138.2, 166.1.

ESIHRMS: Found: *m/z* 495.1805. Calcd for C₃₁H₂₇O₆: (M+H)⁺ 495.1808.

6.5.3 Mo(CO)₆-Mediated Intramolecular Alkoxy carbonylations

General procedure:

A mixture of **10v** or **10w** (0.50 mmol), Mo(CO)₆ (0.0264 g, 0.10 mmol) and NBU₃ (0.102 g, 0.55 mmol) in diglyme (5 mL) was heated at 150 °C for 12 hour under N₂ atmosphere. The solvent was removed under reduced pressure after the reaction was completed and the residue was purified by flash column chromatography (SiO₂, hexane:ethyl acetate = 19:1) to afford the ester products **11v** or **11w**.

Isobenzofuran-1(3*H*)-one (11v).¹²⁵

White solid.

¹H NMR (CDCl₃, 400 MHz) δ 5.31 (s, 2H), 7.48–7.53 (m, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 69.6, 122.1, 125.6, 128.9, 134.0, 146.5, 171.1.

Isochroman-1-one (11w).¹²⁵

Colorless oil.

¹H NMR (CDCl₃, 400 MHz) δ 3.07 (t, J = 6.0 Hz, 2H), 4.54 (t, J = 6.0 Hz, 2H), 7.27 (d, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.54 (dt, J = 1.2, 7.6 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 27.8, 67.3, 125.2, 127.2, 127.6, 130.3, 133.6, 139.5, 165.1.

6.6 Synthesis of 2-Substituted-4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-Mediated Cyclocarbonylation of *o*-Iodoanilines with Aryl Halides

General procedure for Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoaniline with unsaturated halides.

A mixture of *o*-iodoanilines (0.30 mmol), aryl or vinyl halides (0.90 mmol), Mo(CO)₆ (0.60 mmol), and NBU₃ (0.66 mmol) in diglyme (3.0 mL) was heated at 150 °C under N₂ atmosphere. The solvent was removed under reduced pressure after the reaction was completed and the residue was purified by flash column chromatography (SiO₂, hexane:ethyl acetate = 19 : 1 to 10 : 1) to afford pure desired product.

(*E*)-2-Styryl-4*H*-3,1-benzoxazin-4-one (130a).⁶⁴

White solid; mp: 145–147 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1757, 1637, 1593, 1473 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.78 (d, *J* = 16.0 Hz, 1H), 7.38–7.60 (m, 7H), 7.77–7.81 (m, 1H), 7.84 (d, *J* = 16.0 Hz, 1H), 8.20 (dd, *J* = 1.2, 8.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 116.9, 118.8, 126.9, 128.0, 128.1, 128.6, 129.0, 130.3, 134.6, 136.5, 142.0, 147.1, 157.3, 159.3.

ESIHRMS: Found: *m/z* 250.0874. Calcd for C₁₆H₁₂NO₂: (M+H)⁺ 250.0868.

(E)-2-Styryl-6-methyl-4H-3,1-benzoxazin-4-one (13ob).

White solid; mp: 135–137 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1749, 1637, 1591, 1489 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 2.45 (s, 3H), 6.74 (d, J = 16.0 Hz, 1H), 7.36–7.59 (m, 7H), 7.78 (d, J = 16.0 Hz, 1H), 7.99 (s, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 21.2, 116.6, 118.8, 126.7, 127.9, 128.2, 128.9, 130.1, 134.7, 137.7, 138.6, 141.3, 144.9, 156.6, 159.4.

ESIHRMS: Found: m/z 264.1026. Calcd for C₁₇H₁₄NO₂: (M+H)⁺ 264.1025.

(E)-2-Styryl-6-(tert-butyl)-4H-3,1-benzoxazin-4-one (13oc).

Colourless oil;

IR (NaCl, CH₂Cl₂) 1759, 1637, 1591, 1489 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 1.38 (s, 9H), 6.76 (d, J = 16.0 Hz, 1H), 7.36–7.57 (m, 6H), 7.79–7.85 (m, 2H), 8.19 (d, J = 2.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 31.1, 35.0, 116.3, 118.9, 124.6, 126.5, 127.9, 128.9, 130.1, 134.3, 134.7, 141.4, 144.9, 151.9, 156.8, 159.7.

ESIHRMS: Found: m/z 306.1490. Calcd for C₂₀H₂₀NO₂: (M+H)⁺ 306.1494.

(E)-2-Styryl-6-methoxy-4H-3,1-benzoxazin-4-one (13od).

Off-white solid; mp: 144–146 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1749, 1637, 1591, 1490 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 3.89 (s, 3H), 6.75 (d, J = 16.0 Hz, 1H), 7.33–7.42 (m, 4H), 7.51–7.58 (m, 4H), 7.76 (d, J = 16.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 55.9, 108.8, 117.7, 118.8, 125.8, 127.8, 128.4, 128.9, 130.0, 134.8, 140.8, 141.3, 155.4, 159.2, 159.5.

ESIHRMS: Found: m/z 280.0975. Calcd for C₁₇H₁₄NO₃: (M+H)⁺ 280.0974.

(E)-2-Styryl-6-(trifluoromethyl)-4H-3,1-benzoxazin-4-one (13oe).

White solid; mp: 148–150 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1764, 1624, 1591, 1421 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 6.78 (d, J = 16.0 Hz, 1H), 7.41–7.58 (m, 5H), 7.69 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 16.0 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.46 (s, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 117.0, 118.3, 123.2 (q, $^1J_{C-F}$ = 270.8), 126.3 (q, $^3J_{C-F}$ = 4.0 Hz), 127.8, 128.2, 129.1, 130.0 (d, $^2J_{C-F}$ = 33.4 Hz), 130.8, 132.8 (q, $^4J_{C-F}$ = 3.3 Hz), 134.3, 143.7, 149.6, 158.2, 159.0.

ESIHRMS: Found: m/z 318.0753. Calcd for C₁₇H₁₁NO₂F₃: (M+H)⁺ 318.0742.

(E)-2-Styryl-6-chloro-4H-3,1-benzoxazin-4-one (13of).

White solid; mp: 171–173 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1762, 1641, 1469 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 6.77 (d, J = 16.0 Hz, 1H), 7.42–7.60 (m, 6H), 7.74 (dd, J = 4.0, 8.0 Hz, 1H), 7.86 (d, J = 16.0 Hz, 1H), 8.18 (d, J = 4.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 118.0, 118.5, 128.0, 128.1, 128.5, 129.1, 130.5, 133.8, 134.5, 136.8, 142.6, 145.7, 157.5, 158.3.

ESIHRMS: Found: m/z 284.0485. Calcd for C₁₆H₁₁NO₂Cl: (M+H)⁺ 284.0478.

(E)-2-Styryl-6-fluoro-4H-3,1-benzoxazin-4-one (13og).

White solid; mp: 170–172 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1757, 1637, 1593, 1485 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 6.74 (d, J = 16.0 Hz, 1H), 7.39–7.62 (m, 7H), 7.79–7.85 (m, 2H).

¹³C NMR (100 MHz, CDCl₃) δ 114.0 (d, ² J_{C-F} = 24.1 Hz), 118.2 (d, ³ J_{C-F} = 8.7 Hz), 118.5, 124.7 (d, ² J_{C-F} = 23.6 Hz), 128.0, 129.0, 129.2 (d, ³ J_{C-F} = 8.1 Hz), 130.4, 134.5, 142.0, 143.7, 157.6 (d, ¹ J_{C-F} = 187.0 Hz), 160.0, 162.5.

ESIHRMS: Found: m/z 268.0770. Calcd for C₁₆H₁₁NO₂F: (M+H)⁺ 268.0774.

(E)-2-Styryl-6-cyano-4H-3,1-benzoxazin-4-one (13oh).

Yellow solid; mp: 212–214 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 2231, 1762, 1635, 1585, 1481 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 6.79 (d, J = 16.0 Hz, 1H), 7.43–7.62 (m, 5H), 7.68 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 16.0 Hz, 1H), 7.99 (dd, J = 2.0, 8.4 Hz, 1H), 8.49 (d, J = 1.6 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 111.5, 117.3, 117.6, 118.1, 128.1, 128.4, 129.1, 131.0, 133.4, 134.2, 138.7, 144.5, 150.1, 157.4, 159.7.

ESIHRMS: Found: m/z 275.0826. Calcd for C₁₇H₁₁N₂O₂: (M+H)⁺ 275.0821.

(E)-2-Styryl-6-acetyl-4H-3,1-benzoxazin-4-one (13oi).

Light yellow solid; 198–200 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1755, 1674, 1587 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.69 (s, 3H), 6.80 (d, J = 16.0 Hz, 1H), 7.42–7.61 (m, 5H), 7.66 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 16.0 Hz, 1H), 8.38 (dd, J = 2.0, 8.4 Hz, 1H), 8.74 (d, J = 2.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 26.6, 116.7, 118.4, 127.5, 128.2, 129.1, 129.6, 130.8, 134.4, 135.5, 136.2, 143.6, 150.5, 158.8, 159.1, 195.8.

ESIHRMS: Found: m/z 292.0982. Calcd for C₁₈H₁₄NO₃: (M+H)⁺ 292.0974.

(*E*)-2-(4-Methylstyryl)-4*H*-3,1-benzoxazin-4-one (13wa).¹²⁶

White solid; mp: 151–153 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1755, 1635, 1591, 1471 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.37 (s, 3H), 6.72 (d, *J* = 16.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.44–7.47 (m, 3H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.76–7.82 (m, 2H), 8.19 (dd, *J* = 1.2, 8.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 21.4, 116.8, 117.7, 126.8, 128.0 (overlapped), 128.6, 129.7, 131.9, 136.5, 140.8, 142.0, 147.2, 157.5, 159.3.

ESIHRMS: Found: *m/z* 264.1026. Calcd for C₁₇H₁₄NO₂: (M+H)⁺ 264.1025.

(*E*)-2-(2-Methylstyryl)-4*H*-3,1-benzoxazin-4-one (13xa).

White solid; mp: 119–121 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1757, 1635, 1593, 1473 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.50 (s, 3H), 6.71 (d, *J* = 16.0 Hz, 1H), 7.21–7.30 (m, 3H), 7.46–7.50 (m, 1H), 7.61 (t, *J* = 8.0 Hz, 2H), 7.77–7.81 (m, 1H), 8.09 (d, *J* = 16.0 Hz, 1H), 8.21 (dd, *J* = 1.6, 8.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 19.9, 116.9, 120.0, 126.2, 126.4, 126.9, 128.1, 128.6, 130.0, 130.9, 133.6, 136.5, 137.7, 139.5, 147.1, 157.4, 159.3.

ESIHRMS: Found: *m/z* 264.1025. Calcd for C₁₇H₁₄NO₂: (M+H)⁺ 264.1025.

(*E*)-2-(3-Methoxystyryl)-4*H*-3,1-benzoxazin-4-one (13ya).

Light yellow solid; mp: 98–100 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1757, 1637, 1597, 1473 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 3.83 (s, 3H), 6.76 (d, J = 16.0 Hz, 1H), 6.93 (dd, J = 2.0, 7.6 Hz, 1H), 7.09 (t, J = 2.0 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.46–7.50 (m, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.77–7.82 (m, 2H), 8.19 (dd, J = 1.2, 8.0 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 55.2, 112.6, 116.4, 116.9, 119.1, 120.7, 126.9, 128.2, 128.6, 130.0, 135.9, 136.5, 141.9, 147.1, 157.2, 159.2, 159.9.

ESIHRMS: Found: m/z 280.0984. Calcd for C₁₇H₁₄NO₃: (M+H)⁺ 280.0974.

(*E*)-2-(4-Fluorostyryl)-4*H*-3,1-benzoxazin-4-one (13za).¹²⁶

White solid; 158–160 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1757, 1639, 1595, 1473 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 6.71 (d, J = 16.0 Hz, 1H), 7.12 (t, J = 16.0 Hz, 2H), 7.48–7.61 (m, 4H), 7.79–7.84 (m, 2H), 8.22 (dd, J = 1.3, 8.0 Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 116.2 (d, $^2J_{\text{C-F}} = 21.8$ Hz), 116.9, 118.6 (d, $^5J_{\text{C-F}} = 2.2$ Hz), 126.9, 128.2, 128.6, 129.8 (d, $^3J_{\text{C-F}} = 8.3$ Hz), 130.9 (d, $^4J_{\text{C-F}} = 3.5$ Hz), 136.6, 140.6, 147.1, 158.2 (d, $^1J_{\text{C-F}} = 208.0$ Hz), 162.6, 165.1.

ESIHRMS: Found: m/z 268.0770. Calcd for $\text{C}_{16}\text{H}_{11}\text{NO}_2\text{F}$: $(\text{M}+\text{H})^+$ 268.0774.

(*E*)-2-(4-(*tert*-tutyl)Styryl)-4*H*-3,1-benzoxazin-4-one (13aba).

Light yellow solid; 146–148 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1755, 1635, 1593, 1473 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 1.34 (s, 9H), 6.76 (d, $J = 16.0$ Hz, 1H), 7.43–7.60 (m, 6H), 7.76–7.81 (m, 1H), 7.84 (d, $J = 16.0$ Hz, 1H), 8.20 (dd, $J = 1.2, 8.0$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 31.1, 34.9, 116.9, 117.9, 126.0, 126.8, 127.9, 128.0, 128.6, 131.9, 136.5, 141.9, 147.2, 153.9, 157.5, 159.4.

ESIHRMS: Found: m/z 306.1495. Calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_2$: $(\text{M}+\text{H})^+$ 306.1494.

(*E*)-2-(4-Methoxystyryl)-4*H*-3,1-benzoxazin-4-one (13aca).¹²⁶

Light yellow solid; mp: 152–154 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1751, 1635, 1589 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 3.84 (s, 3H), 6.64 (d, J = 16.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 2H), 7.44–7.58 (m, 4H), 7.76–7.82 (m, 2H), 8.09 (dd, J = 1.2, 7.6 Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 55.4, 114.5, 116.3, 116.8, 126.7, 127.4, 127.8, 128.6, 129.7, 136.5, 141.7, 147.3, 157.7, 159.5, 161.5.

ESIHRMS: Found: m/z 280.0974. Calcd for $\text{C}_{17}\text{H}_{14}\text{NO}_3$: $(\text{M}+\text{H})^+$ 280.0974.

(*E*)-2-(4-Phenylbut-1-en-1-yl)-4*H*-3,1-benzoxazin-4-one (13ada).

Colourless oil; IR (NaCl, CH_2Cl_2) 1759, 1653, 1598, 1473 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 2.62–2.68 (m, 2H), 2.85 (t, J = 8.0 Hz, 2H), 6.18 (dt, J = 1.6, 16.0 Hz, 1H), 7.13–7.33 (m, 6H), 7.46–7.50 (m, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.76–7.80 (m, 1H), 8.19 (dd, J = 1.2, 8.0 Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 34.47, 34.48, 117.0, 122.5, 126.2, 126.8, 128.1, 128.3, 128.5, 128.6, 136.5, 140.6, 145.9, 147.0, 156.7, 159.4.

ESIHRMS: Found: m/z 278.1187. Calcd for $\text{C}_{18}\text{H}_{16}\text{NO}_2$: $(\text{M}+\text{H})^+$ 278.1181.

2-Phenyl-4*H*-3,1-benzoxazin-4-one (13aa).⁶⁴

White solid; mp: 119–121 $^{\circ}\text{C}$ (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1759, 1624, 1573, 1473, 1315 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.49–7.59 (m, 4H), 7.69 (d, $J = 8.0$ Hz, 1H), 7.82 (t, $J = 8.0$ Hz, 1H), 8.24 (d, $J = 8.0$ Hz, 1H), 8.31 (d, $J = 8.0$ Hz, 2H).

^{13}C NMR (100 MHz, CDCl_3) δ 117.0, 127.2, 128.2, 128.3, 128.5, 128.7, 130.2, 132.6, 136.5, 146.9, 157.1, 159.5.

ESIHRMS: Found: m/z 224.0719. Calcd for $\text{C}_{14}\text{H}_{10}\text{NO}_2$: $(\text{M}+\text{H})^+$ 224.0712.

2-(4-Methoxyphenyl)-4*H*-3,1-benzoxazin-4-one (13ha).^{62d}

White solid; mp: 147–149 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1759, 1514 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 3.88 (s, 3H), 6.98 (d, $J = 8.4$ Hz, 2H), 7.46 (t, $J = 7.6$ Hz, 1H), 7.62 (d, $J = 7.6$ Hz, 1H), 7.78 (t, $J = 8.0$ Hz, 1H), 8.20 (d, $J = 7.6$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 2H).

^{13}C NMR (100 MHz, CDCl_3) δ 55.5, 114.1, 116.7, 122.5, 126.9, 127.6, 128.5, 130.2, 136.4, 147.3, 157.0, 159.7, 163.2.

ESIHRMS: Found: m/z 254.0819. Calcd for $\text{C}_{15}\text{H}_{12}\text{NO}_3$: $(\text{M}+\text{H})^+$ 254.0817.

2-(4-Acetylphenyl)-4*H*-3,1-benzoxazin-4-one (13ba).

White solid; mp: 177–179 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1762, 1685, 1606, 1473 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.66 (s, 3H), 7.55 (t, J = 7.6 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.4 Hz, 2H), 8.25 (d, J = 8.4 Hz, 1H), 8.39 (d, J = 8.0 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃) δ 26.8, 117.1, 127.5, 128.47, 128.5, 128.7, 128.8, 134.1, 136.7, 139.8, 146.6, 156.0, 159.1, 197.4.

ESIHRMS: Found: m/z 266.0816. Calcd for C₁₆H₁₂NO₃: (M+H)⁺ 266.0817.

2-(*p*-Tolyl)-4*H*-3,1-benzoxazin-4-one (13aea).^{62d}

White solid; mp: 152–154 °C (CH₂Cl₂).

IR (NaCl, CH₂Cl₂) 1759, 1608, 1473 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.43 (s, 3H), 7.30 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 8.4 Hz, 1H), 8.19 (d, J = 8.0 Hz, 2H), 8.22 (d, J = 7.6 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 21.6, 116.9, 127.1, 127.4, 127.9, 128.3, 128.5, 129.5, 136.4, 143.3, 147.1, 157.3, 159.6.

ESIHRMS: Found: m/z 238.0869. Calcd for $C_{15}H_{12}NO_2$: $(M+H)^+$ 238.0868.

Ethyl 4-(4-oxo-4*H*-3,1-benzoxazin-4-one-2-yl)benzoate (13ga).

White solid; mp: 128–130 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1764, 1714, 1624, 1473 cm^{-1} .

1H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, $J = 7.2$ Hz, 3H), 4.41 (q, $J = 7.2$ Hz, 2H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 1H), 7.81–7.85 (m, 1H), 8.14 (d, $J = 8.4$ Hz, 2H), 8.22 (d, $J = 8.0$ Hz, 1H), 8.34 (d, $J = 8.4$ Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 61.4, 117.0, 127.4, 128.1, 128.6, 128.7, 129.7, 133.8, 134.0, 136.6, 146.6, 156.1, 159.1, 165.7.

ESIHRMS: Found: m/z 296.0930. Calcd for $C_{17}H_{14}NO_4$: $(M+H)^+$ 296.0923.

2-(4-Fluorophenyl)-4*H*-3,1-benzoxazin-4-one (13afa).⁶¹

Off-white solid; mp: 170–172 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1761, 1625, 1510, 1421 cm^{-1} .

1H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, $J = 8.4$ Hz, 2H), 7.52 (t, $J = 7.6$ Hz, 1H), 7.68 (d, $J = 8.0$ Hz, 1H), 7.83 (t, $J = 7.6$ Hz, 1H), 8.24 (d, $J = 8.0$ Hz, 1H), 8.31–8.35 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3) δ 116.0 (d, $^2J_{\text{C-F}} = 22.0$ Hz), 116.9, 126.5 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 127.2, 128.3, 128.6, 130.7 (d, $^3J_{\text{C-F}} = 9.1$ Hz), 136.6, 146.9, 157.8 (d, $^1J_{\text{C-F}} = 314.0$ Hz), 164.3, 166.9.

ESIHRMS: Found: m/z 242.0624. Calcd for $\text{C}_{14}\text{H}_9\text{NO}_2\text{F}$: $(\text{M}+\text{H})^+$ 242.0617.

2-(*o*-Tolyl)-4*H*-3,1-benzoxazin-4-one (13aga).^{62d}

Off-white solid; mp: 112–114 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1759, 1608, 1473 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 2.73 (s, 3H), 7.31–7.45 (m, 3H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 1H), 7.83 (t, $J = 8.0$ Hz, 1H), 8.03 (d, $J = 7.6$ Hz, 1H), 8.25 (d, $J = 8.0$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 22.1, 116.8, 126.0, 127.2, 128.36, 128.41, 129.8, 130.1, 131.5, 131.9, 136.5, 139.1, 146.8, 158.3, 159.7.

ESIHRMS: Found: m/z 238.0869. Calcd for $\text{C}_{15}\text{H}_{12}\text{NO}_2$: $(\text{M}+\text{H})^+$ 238.0868.

2-(Thiophen-3-yl)-4*H*-3,1-benzoxazin-4-one (13ia).

Off-white solid; mp: 123–125 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1759, 1622, 1604, 1473 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.39–7.41 (m, 1H), 7.49 (t, $J = 7.6$ Hz, 1H), 7.64 (d, $J = 8.4$ Hz, 1H), 7.78–7.82 (m, 2H), 8.21 (d, $J = 8.0$ Hz, 1H), 8.27 (d, $J = 2.8$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 116.9, 126.7, 127.0 (overlapped), 128.0, 128.6, 130.7, 133.3, 136.5, 147.1, 153.9, 159.4.

ESIHRMS: Found: m/z 230.0283. Calcd for $\text{C}_{12}\text{H}_8\text{NO}_2\text{S}$: $(\text{M}+\text{H})^+$ 230.0276.

2-(Naphthalen-1-yl)-4*H*-3,1-benzoxazin-4-one (13da).¹²⁷

White solid; mp: 131–133 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1761, 1604, 1473 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.57–7.70 (m, 4H), 7.80–7.91 (m, 2H), 7.94 (d, $J = 8.0$ Hz, 1H), 8.06 (d, $J = 8.4$ Hz, 1H), 8.33 (dt, $J = 1.2, 7.6$ Hz, 2H), 9.15 (d, $J = 8.4$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 116.9, 124.7, 125.7, 126.3, 126.9, 127.4, 127.8, 128.47, 128.54, 128.8, 130.0, 130.7, 133.1, 134.0, 136.5, 146.7, 157.6, 159.7.

ESIHRMS: Found: m/z 274.0869. Calcd for $\text{C}_{18}\text{H}_{12}\text{NO}_2$: $(\text{M}+\text{H})^+$ 274.0868.

***N*-(2-Iodophenyl)cinnamamide (14).**¹²⁸

White solid; mp: 147–149 °C (CH_2Cl_2).

IR (NaCl, CH_2Cl_2) 1685, 1631, 1519, 1431 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 6.59 (d, $J = 15.6$ Hz, 1H), 6.87 (t, $J = 8.0$ Hz, 1H), 7.34–7.44 (m, 4H), 7.58–7.61 (m, 2H), 7.63 (br s, 1H), 7.77–7.81 (m, 2H), 8.38 (d, $J = 7.6$ Hz, 1H).

^{13}C NMR (CDCl_3 , 100 MHz) δ (ppm) 90.1, 120.6, 122.0, 126.0, 128.1, 128.9, 129.3, 130.2, 134.4, 138.3, 138.8, 143.0, 163.9.

ESIHRMS: Found: m/z 350.0038. Calcd for $\text{C}_{15}\text{H}_{13}\text{NOI}$: $(\text{M}+\text{H})^+$ 350.0042.

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Summary and Perspective

In this thesis, the author described efficient amino/alkoxycarbonylation of aryl halides mediated by group VI metal carbonyl complexes. The drawback for the conventional palladium catalysed three-component coupling reaction between aryl halides, CO gas, and amines or alcohols to provide amides and esters is that the toxic gaseous carbon monoxide is required in the reaction system, and sometimes high pressure of CO gas is necessary for efficient conversion. In the group VI metal carbonyl complexes mediated amino/alkoxycarbonylation of aryl halides, the metal carbonyl complexes can be used both as the CO source and catalyst, thus the toxic CO gas can be avoided.

In chapter 2, benzyl amine tungsten carbonyl complex was used as the carbamoyl anion equivalent, by treating with base, which can be converted to carbamoyl tungsten intermediate **A**. The intermediate **A** reacts with aryl halides in the presence of palladium acetate to give amides in moderate to excellent yield. The carbamoyl tungsten intermediate **A** could be trapped by norbornene to give the carbamoyl substituted norbornene products (Scheme 1). The mechanism for the Pd-catalyzed carbamoylation of aryl halides may include the transmetalation between the carbamoyltungsten intermediate and aryl palladium intermediate.

Scheme 1. Palladium-catalyzed carbamoylation of aryl halides by tungsten carbonyl amine complex

In chapter 3, the carbamoylation of aryl halides can be carried out even without palladium catalyst through increasing the reaction temperature. The benzyl amine tungsten carbonyl complex was not only used as the CO and amine source but also used as the catalyst. The carbamoyl intermediate was also trapped with norbornene to give the carbamoyl norbornene product (Scheme 2).

Scheme 2. Carbamoylation of aryl halides by molybdenum or tungsten carbonyl amine complexes

In chapter 4, to simplify the reaction procedure, the author tried to use one pot manner for the carbamoylation of aryl halide. The mixture of the Mo(CO)_6 , aryl halides, amines and the base in diglyme was heated at 150°C for several hours to give the amides in good to excellent yields. Furthermore, this protocol was also applied for esters preparation from the corresponding alcohols and aryl halides (Scheme 3).

Scheme 3. Mo(CO)_6 -mediated carbamoylation and alkoxy carbonylation of aryl halides

The Mo(CO)_6 -mediated carbamoylation and alkoxy carbonylation of aryl halides can be applied to synthesize lactams and lactones through intramolecular carbonylation (Scheme 4). Furthermore, primary amides and carboxylic acids can be synthesized through this methodology by employing the ammonia solution and water as the coupling partner, respectively (Scheme 5).

Scheme 4. Lactams and lactones formation by intramolecular carbonylation

Scheme 5. Mo(CO)₆-mediated carboxylic acid and primary amide synthesis

In chapter 5, the author applied this protocol for preparation of the 2-substituted-4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoanilines with aryl or vinyl halides (Scheme 6). The mechanism for this reaction included twice carbonyl insertion to form the intermediate **B** and **F** (Scheme 7). The product incorporated two molecules of CO from Mo(CO)₆.

Scheme 6. Preparation of the 2-substituted-4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-mediated cyclocarbonylation of *o*-iodoanilines with aryl halides

Scheme 7. The proposed mechanism for Mo(CO)_6 -mediated cyclocarbonylation of *o*-iodoanilines with aryl halides

Although this amino/alkoxycarbonylation of aryl halides mediated by group VI metal carbonyl complexes is quite efficient for preparing various amides and esters, it still has some limitations. For examples, the bulky alcohols such as tertiary butyl alcohol couldn't be converted to the corresponding ester due to the steric hindrance. Additionally, when this methodology was tried to carry out in catalytic aminocarbonylation under CO atmosphere, the yields of the amides is quite low (Section 4.2.1). This is probably due to the fact that the carbon monoxide gas suppressed the CO ligand releasing from

molybdenum centre, thus the oxidative addition of phenyl iodide to molybdenum was inhibited.

In spite of these limitations, the present synthetic methods by using group VI metal carbonyl complex to construct amides and esters from aryl halides developed in this thesis are expected to be further applicable in the preparation of various types of arylcarboxamidine and arylcarboximidic esters by changing the CO to isonitrile $M(CNR)_6$ ($M = Cr, Mo, W$) (Scheme 8).

Scheme 8. Mo(CNR)_6 -mediated arylcarboxamidine and arylcarboximidic ester formation

List of Publications

1. **Wei Ren**, and Motoki Yamane* “Palladium-Catalyzed Carbamoylation of Aryl Halides by Tungsten Carbonyl Amine Complex” *J. Org. Chem.* **2009**, 74, 8332–8335. (Highlighted in *SynFacts*, **2010**, 0217.)
2. **Wei Ren**, and Motoki Yamane* “Carbamoylation of Aryl Halides by Molybdenum or Tungsten Carbonyl Amine Complexes” *J. Org. Chem.* **2010**, 75, 3017–3020. (Highlighted in *ChemInform*, **2010**, 41 (37).)
3. **Wei Ren**, and Motoki Yamane* “Mo(CO)₆-Mediated Carbamoylation of Aryl Halides” *J. Org. Chem.* **2010**, 75, 8410–8415.
4. **Wei Ren**, A Emi, and Motoki Yamane* “Mo(CO)₆-Mediated Alkoxy carbonylation of Aryl Halides” *Synthesis* **2011**, 2303–2309.
5. **Wei Ren**, Chuan Zhu, and Motoki Yamane* “Synthesis of 2-Substituted-4*H*-3,1-benzoxazin-4-ones by Mo(CO)₆-Mediated Cyclocarbonylation of *o*-Iodoanilines with Aryl or Vinyl Halides”
To be submitted