Highly Efficient Transformations of Carbonyl Compounds Catalyzed by Iridium Complexes

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Contents

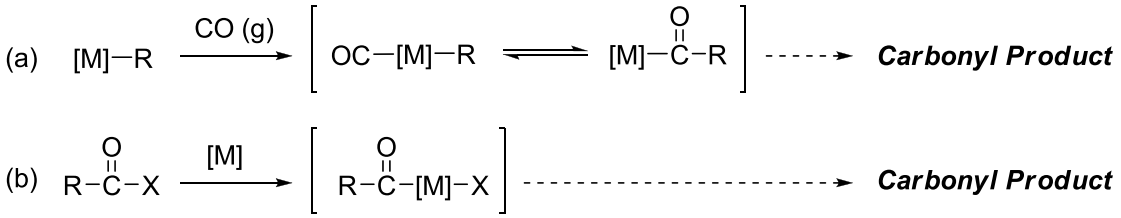
Abbreviations

Ac	acetyl
Binap	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Biphep	2,2'-bis(diphenylphosphino)-1,1'-biphenyl
Cod	1,5-cyclooctadiene
Cy	cyclohexyl
Cp*	η^5-pentamethylcyclopentadienyl
DFT	density functional theory
DIT	dithranol
DME	1,2-dimethoxyethane
DMPU	*N*,*N*'-dimethylpropyleneurea
Dppbz	1,2-bis(diphenylphosphino)benzene
Dppe	1,2-bis(diphenylphosphino)ethane
Dppf	1,1'-bis(diphenylphosphino)ferrocene
Dppm	1,1'-bis(diphenylphosphino)methane
Dppp	1,3-bis(diphenylphosphino)propane
Dtbpy	4,4'-di-*tert*-butylbipyridine
IMes	1,3-dimesitylimidazol-2-ylidene
IPr	1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene
Mes	mesityl
MePhos	2-dicyclohexylphosphino-2'-methylbiphenyl
NHC	*N*-heterocyclic carbene
NMP	*N*-methylpyrrolidone
Py	pyridyl
RuPhos	2-dicyclohexylphosphino-2',6'-diisopropoxybiphenyl
SPhos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
Tol	tolyl
Ts	tosyl
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
XPhos	2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

General Introduction

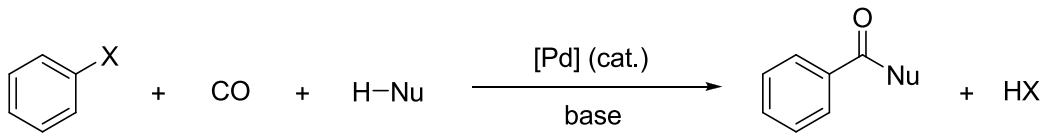
Transition-metal-catalyzed transformation of carbonyl compounds

Carbonyl compounds are widespread and universal functional groups appearing in natural products as well as artificial molecules. Therefore, development of highly efficient and selective transformation of carbonyl functionalities is indispensable for green chemistry. Transition-metal-catalyzed transformation to produce various kinds of carbonyl compounds is one of the most powerful synthetic tools. The reaction would be classified broadly to two types; 1) Use of carbon monoxide as a carbonyl source (Scheme 1-a), and 2) Use of carbonyl compounds as substrates (Scheme 1-b).



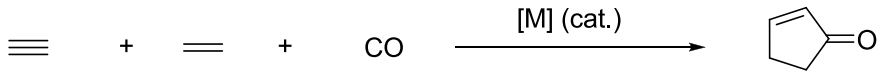
Scheme 1. General reaction types of transition-metal-catalyzed transformation of carbonyl functionalities.

The former carbonylation reaction has been intensively studied and a wide variety of carbonyl compounds can be synthesized.[1] For example, the reaction of aromatic halides and appropriate nucleophiles in the presence of carbon monoxide is performed to prepare carbonyl compounds using a catalytic amount of a palladium complex (Scheme 2).[2] Also, cyclocarbonylations were well studied by using various transition-metal catalysts (Scheme 3).[3,4] However, these methods suffer from difficulty of handling highly toxic and gaseous carbon monoxide.[5]



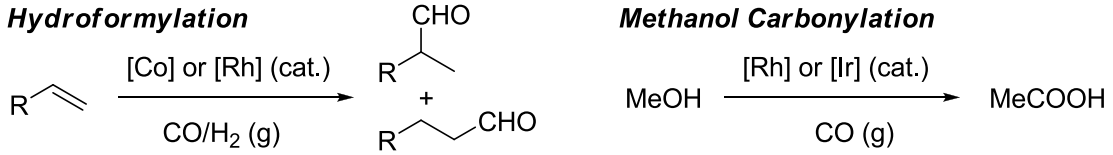
X = Cl, Br, I, OTs, ... Nu = OH, OR, NR_2, ...

Scheme 2. Palladium-catalyzed carbonylation of aryl halides with various nucleophiles.



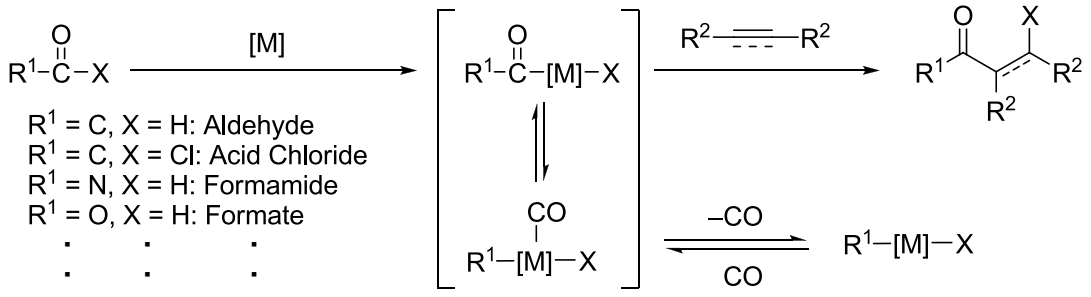
Scheme 3. [2+2+1] carbonylative cycloaddition reaction.

The carbonylation using carbon monoxide has been widely used in industrial chemistry. Hydroformylation is one of the most important synthetic processes of aldehydes from alkenes, carbon monoxide and hydrogen (Scheme 4). In 1938, the original cobalt complex $Co_2(CO)_8$ was developed by Otto Roelen.[6] Since the 1970's, more effective rhodium catalysts were applicable to the hydroformylation.[7] Unsaturated hydride-carbonyl complex would be an active species to insert olefines. Subsequent carbonylation followed by reductive elimination between C(O)–H bond affords the aldehydes and active metal species regenerates. Furthermore, most of acetic acid is produced by methanol carbonylation in the presence of rhodium catalysts (Scheme 4).[8] In the late 1990s, more greener and efficient iridium complex, namely Cativa catalyst ($[Ir(CO)_2I_2]^-$), was developed and has been in practical use for the methanol carbonylation.[9]



Scheme 4. Hyroformylation and methanol carbonylation.

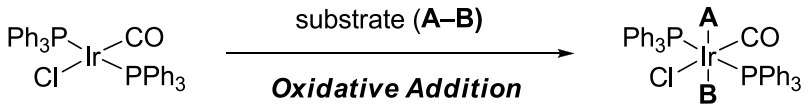
The latter is an attractive method for direct transformation of carbonyl compounds (Scheme 1-b). One of them, transition-metal-catalyzed addition of carbonyl compounds to carbon-carbon unsaturated bonds such as alkynes and alkenes is environmentally friendly because all atoms of the substrates are retained in the products (Scheme 5).[10] To date, various types of addition of carbonyl functionalities to multiple bonds have been developed.[11,12] For example, the addition of aldehydes (R^1 = C, X = H) to alkynes or alkenes, hydroacylation,[11] has been intensively studied, although efficiency of the reaction is not so high. Suppressing the decarbonylation is generally difficult, and carbon monoxide must be pressurized to avoid decarbonylation or appropriate directing groups were often indispensable for successful reactions.



Scheme 5. Additions of carbonyl functionalities to carbon-carbon multiple bonds.

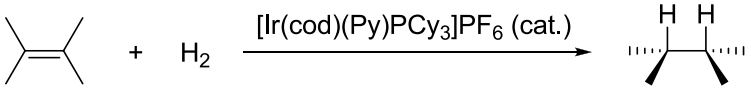
Development of iridium catalyst

In general, the carbon-metal bond in a third-row transition-metal complex is believed to be likely more stable than that in a first- or second-row transition-metal complex. Thus, third-row transition-metal complex is often too stable as a catalyst in organic synthesis. Especially, iridium complexes have been used as model compounds to acquire an understanding of the elementary steps of transition-metal-catalyzed reaction. Oxidative addition has been studied closely by using $IrCl(CO)(PPh_3)_2$, namely Vaska's complex (Scheme 6).[13] This chemistry greatly contributed to the development of organometallic chemistry as well as catalytic organic synthesis.



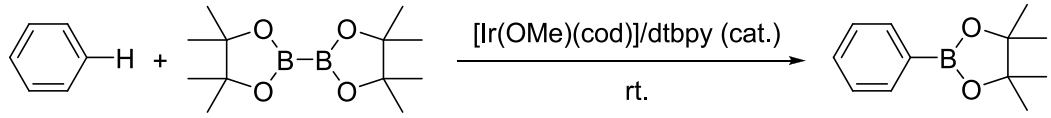
Scheme 6. Oxidative addition of a substrate (**A**–**B**) to $IrCl(CO)(PPh_3)_2$.

Since a breakthrough in the study of alkene hydrogenation by using $[Ir(cod)(Py)PCy_3]PF_6$ (Scheme 7),[14] various iridium-catalyzed reactions have been developed to date.[15] Iridium complexes have high abilities of hydrogen transfer and are widely applicable in the area of chemoselective and enantioselective hydrogenation.



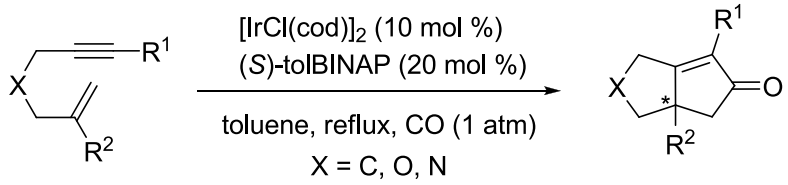
Scheme 7. Alkene hydrogenation catalyzed by $[Ir(cod)(Py)PCy_3]PF_6$.

Although progress in iridium-catalyzed carbon-carbon or carbon-heteroatom bond formation have lagged far behind compared to other transition-metal catalysts such as rhodium and palladium, due to their stability of the complex. Several useful reactions for organic synthesis were reported in the early 1990s. For example, in catalytic C–H borylation, iridium catalysts must be efficient under mild conditions with a distinctive stability and catalytic control (Scheme 8).[16] Boryl compounds thus obtained are valuable building-blocks for C–C bond formations in the palladium-catalyzed Suzuki-Miyaura coupling reaction.[17]



Scheme 8. Iridium-catalyzed C–H borylation.

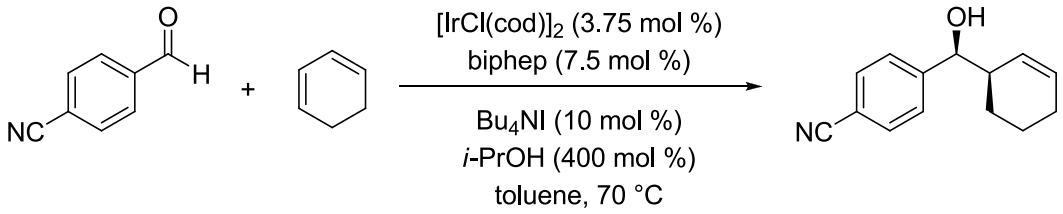
Also, the iridium-catalyzed transformations of carbonyl functionalities with the C–C bond formation have been reported. In 2000, Shibata reported the iridium-catalyzed enatioselective Pauson-Khand-type reaction of enynes under CO atmosphere to afford bicyclic cyclopentenones (Scheme 9).[18] Subsequently, aldehydes could be used as an efficient CO source, instead of the toxic CO gas.[5,19]



Scheme 9. Iridium-catalyzed enatioselective Pauson-Khand-type reaction of enynes.

In the methanol carbonylation,[9] as mentioned in Scheme 4, the iridium system is more practical than its rhodium counterpart and leads to higher reaction rates, a reduced formation of byproducts, and better yield on CO.

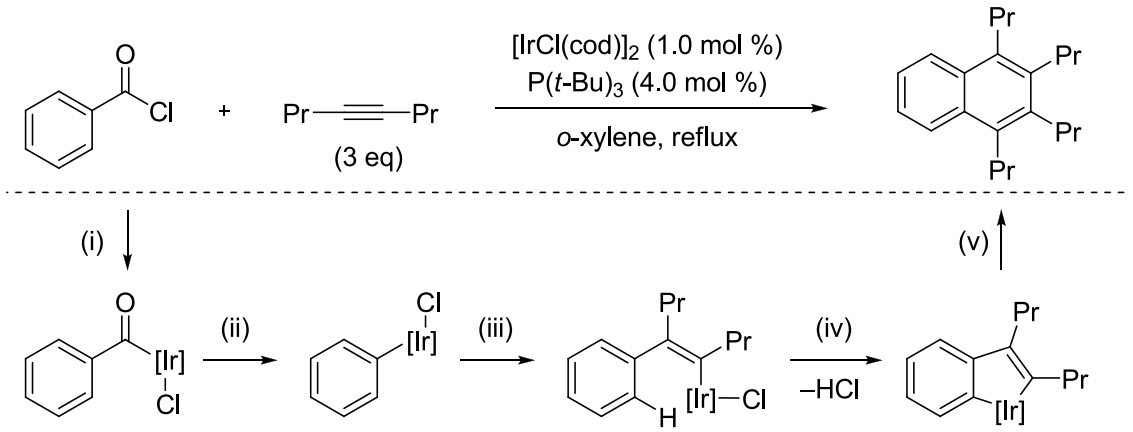
Recently, hydrogen-mediated reductive C–C bond formation reactions have been developed in the absence of stoichiometric organometallic reagents or metallic reductants.[20] For examples, Krishce reported that the iridium-catalyzed transfer hydrogenative coupling of 1,3-diene and aldehyde with *i*-PrOH as a hydrogen source (Scheme 10).[21] Similar strategies have been applied to ruthenium catalyst systems.[22]



Scheme 10. Iridium-catalyzed transfer hydrogenative coupling of 1,3-diene and aldehyde.

In the $[IrCl(cod)]_2/P(t\text{-}Bu)_3$ catalyst system, aroyl chlorides reacted with two internal alkynes to provide polysubstituted naphthalenes via decarbonylation (Scheme 11).[23]

The reaction would proceed as follows; (i) oxidative addition of aroyl chloride to Ir(I); (ii) decarbonylation of the acyl-Ir(III) intermediate; (iii) insertion of alkynes into Ir–C bond; (iv) *ortho*-iridation with the elimination of HCl; and (v) insertion of the second alkyne followed by reductive elimination to give the product.

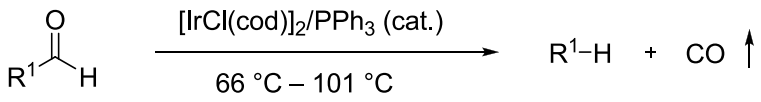


Scheme 11. Iridium-catalyzed reaction of aroyl chlorides with internal alkynes.

Overview of the present Thesis

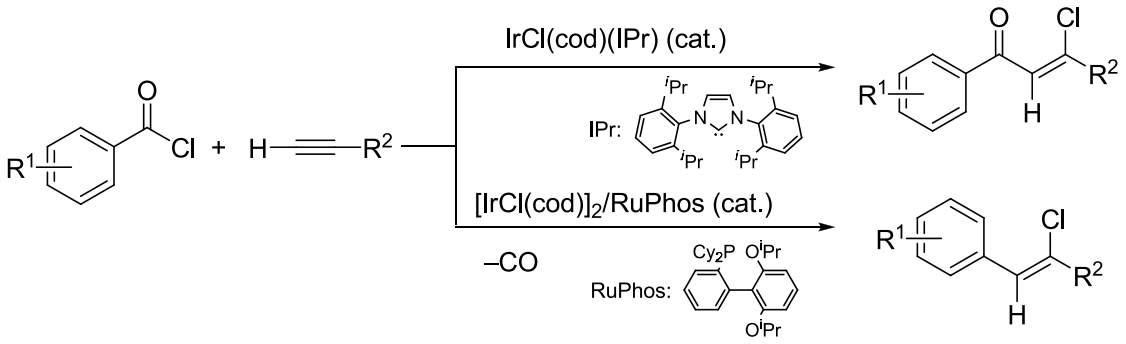
With these backgrounds in mind, the author anticipated that the iridium complex would stabilize the putative acyl-intermediate effectively and following insertion of carbon-carbon unsaturated bonds would proceed smoothly to give addition products without decarbonylation. The present Thesis demonstrates that altitude control of reactivities of acyl complexes and highly efficient transformations of carbonyl compounds by using iridium catalysts, such as addition and annulation of carbonyl functionalities to alkynes.

In Chapter 1, the author describes an iridium-catalyzed decarbonylation of aldehydes which was found during the course of the development of hydroacylation (Scheme 12).[24] The combination of easily accessible $[IrCl(cod)]_2$ with monodentate phosphines such as PPh_3 or $P(n\text{-}Bu)_3$ efficiently catalyzes the reaction under mild conditions as compared to conventional rhodium catalysts. Furthermore, the iridium catalyst system is unnecessary to use any chemical scavenger of CO. This practical method should be widely applicable to various substrates with functional-group compatibility.

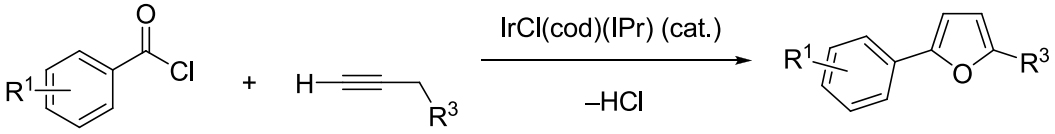


Scheme 12. Iridium-catalyzed decarbonylation of aldehydes.

The addition of acid chlorides to alkynes can introduce both the carbonyl and the chloro functionalities simultaneously. However, the carbonyl functionality is often lost during the catalysis via facile decarbonylation steps. In Chapter 2, the author discloses an iridium *N*-heterocyclic carbene (NHC) complex, IrCl(cod)(IPr), successfully catalyzes an addition of common aromatic acid chlorides to terminal alkynes to afford (*Z*)-*β*-chloro-*α*,*β*-unsaturated ketones with regio- and stereoselectivity (Scheme 13).[25] By changing the NHC (IPr) ligand to a phosphine (RuPhos), the addition occurs with the decarbonylation to give the corresponding (*Z*)-vinyl chlorides. Furthermore, the former reaction using IrCl(cod)(IPr) can be applied to a catalytic synthesis of 2,5-disubstituted furans (Scheme 14).

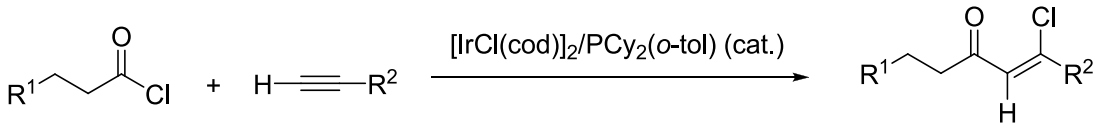


Scheme 13. Iridium-catalyzed addition of aromatic acid chlorides to terminal alkynes.



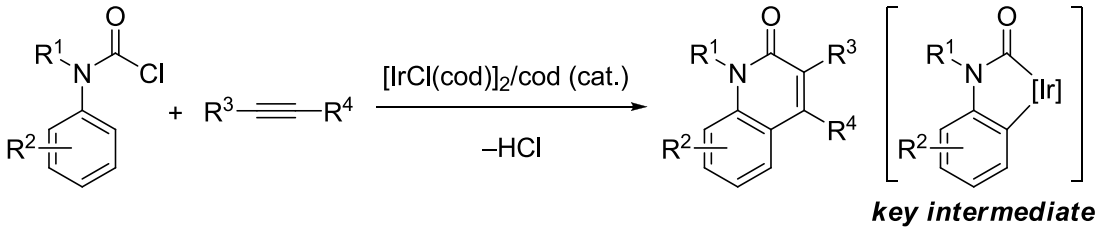
Scheme 14. Iridium-catalyzed synthesis of 2,5-disubstituted furans.

As described in Chapter 3, the addition of aliphatic acid chlorides to terminal alkynes without decarbonylation is realized by using [IrCl(cod)]$_2$/PCy$_2$(*o*-tol) catalyst system (Scheme 15).[26] Even as using alkyl acid chlorides having *β*-hydrogen on the sp^3 carbon, the reaction smoothly proceeds to afford corresponding *β*-chloroalkenyl ketones in high yields and *Z*-selectivity. Addition products are useful intermediates for constructing various heterocycles.



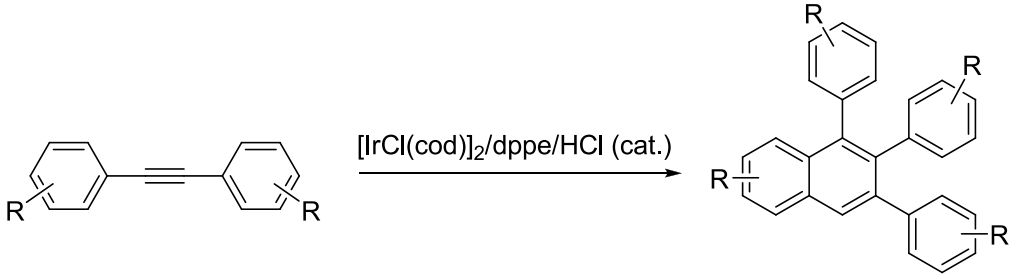
Scheme 15. Iridium-catalyzed addition of aliphatic acid chlorides to terminal alkynes.

In Chapter 4, the author demonstrated that an iridium complex successfully catalyzes the annulations of various *N*-arylcarbamoyl chlorides with internal alkynes to afford 2-quinolones in high yields (Scheme 16).[27] The present reaction is widely applicable to substrates with various functionalities. As for a stoichiometric reaction of $[IrCl(cod)]_2$ and a carbamoyl chloride with PPh_3 as an additive, a five-membered amide-iridacycle complex was isolated and the structure was confirmed by X-ray diffraction analysis. It is likely that such an iridacycle species is a key intermediate in the catalytic reaction.



Scheme 16. Iridium-catalyzed annulation of *N*-arylcarbamoyl chlorides with internal alkynes.

Chaper 5 deals with an iridium-catalyzed cyclodimerization of diarylacetylenes to prepare multisubstituted naphthalenes (Scheme 17).[28] The use of HCl as an additive is essential to generate an iridium-hydride species as a key intermediate. The reaction would start from insertion of diarylalkynes to the iridium-hydride species. A wide variety of diarylacetylenes can be applied to the reaction affording the multisubstituted naphthalenes in good to high yields.



Scheme 17. Iridium-catalyzed cyclodimerization of diarylacetylenes.

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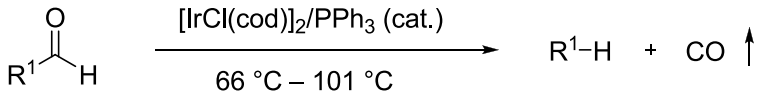
Chapter 1

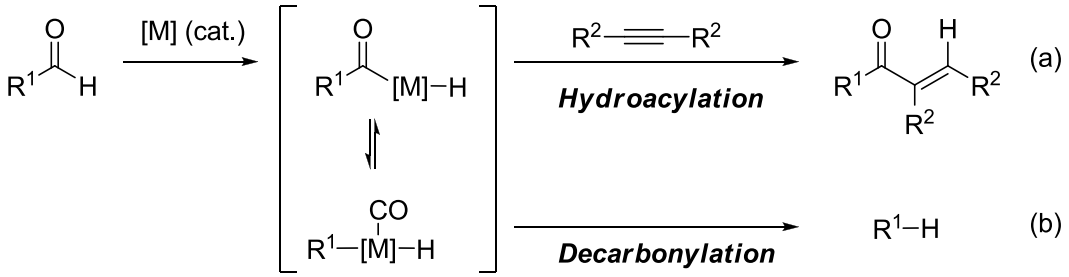
Iridium-Catalyzed Decarbonylation of Aldehydes under Mild Conditions

The iridium-catalyzed decarbonylation reaction of aldehydes using a catalytic amount of commercially available $[IrCl(cod)]_2$ and an easily accessible monodentate phosphine such as PPh_3 and $P(n\text{-}Bu)_3$ was developed. The reaction proceeded smoothly at lower temperatures (66–101 °C) and without any chemical scavenger of CO. This practical and reliable method should be widely applicable to various substrates with excellent functional-group compatibility.



1-1. Introduction

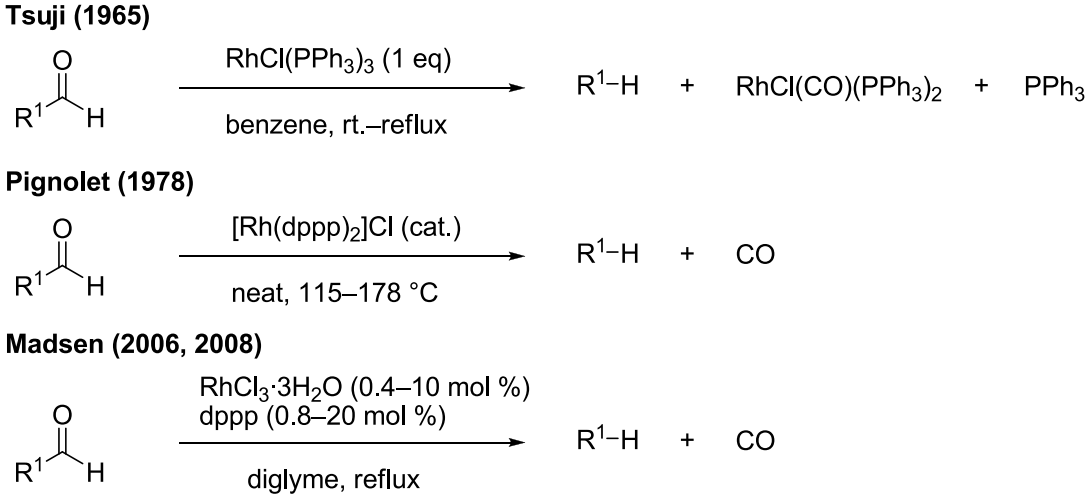
Oxidative addition to the carbon–hydrogen C(O)–H bond of aldehyde is an important step for activation and utilization of aldehydes as substrates. In case that the resulting acylmetal intermediates react with carbon–carbon unsaturated bonds followed by reductive elimination, hydroacylation can be established (Scheme 1-1-a).[1] To suppress the decarbonylation step (Scheme 1-1-b), external carbon monoxide or appropriate directing groups is often indispensable for successful reaction. Although iridium complexes are likely favorable to hydroacylation because the stability of the carbon–metal bond on the putative acyl intermediate, there is only one report for the direct iridium-catalyzed hydroacylation of alkynes with aldehydes.[2] Therefore, the author began investigations of the iridium catalysis with aldehydes aimed at hydroacylation and he developed iridium-catalyzed decarbonylation of aldehydes under mild conditions.



Scheme 1-1. Transition-metal-catalyzed reactions of aldehydes.

The removal of formyl functionalities, decarbonylation of aldehydes, is one of the essential protocols of synthetic chemistry, including in the total syntheses of natural products.[3] The decarbonylation reaction of aldehydes was first discovered by Tsuji and Ohno using a stoichiometric amount of Wilkinson's complex, $RhCl(PPh_3)_3$ (Scheme 1-2).[4] As for catalytic reactions, Doughty and Pignolet found that rhodium complexes with chelating diphosphines were much more reactive as catalysts.[5] Since then, rhodium catalysts with chelating phosphines have been extensively studied in decarbonylation reactions of aldehydes.[6] Recently, Madsen and co-workers reported a mechanism for the rhodium-catalyzed decarbonylation of aldehydes by DFT calculations.[7a] They mentioned that the reaction involves a rapid oxidative addition into the C(O)–H bond, followed by a rate-limiting extrusion of CO. Some Pd[8] and Ru,[9] as well as Ir,[10] complexes were also reported as catalysts for decarbonylation and related reactions. However, in order to realize the efficient catalytic (or even stoichiometric) decarbonylation of aldehydes, elevated reaction temperatures (typically

>160 °C)[3a,b,g,5,6a,b,d,7a,8] or an associated chemical scavenger of the evolved CO (*i.e.*, by an accompanying carbonylation reaction[6c,10,11] or with added diphenylphosphoryl azide[12] to remove the evolved CO) are indispensable. Actually, more than a stoichiometric, not a catalytic, amount of $RhCl(PPh_3)_3$ is still being used to obtain efficient decarbonylations of aldehyde functionalities as an important step in various total syntheses.[3a–g] Hence, a much more active catalyst system to realize the reliable catalytic decarbonylation of aldehydes at lower temperatures, and without a chemical scavenger for CO, is highly desirable.



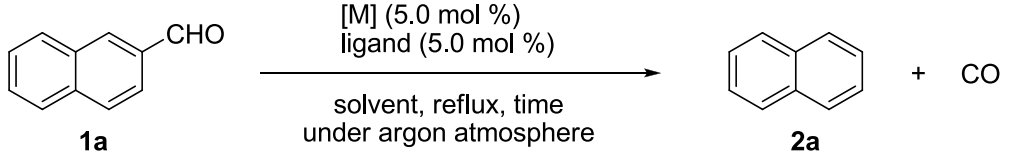
Scheme 1-2. Rhodium-mediated or -catalyzed decarbonylation of aldehydes.

1-2. Result and Discussion

Firstly, the decarbonylation of 2-naphthaldehyde (**1a**) was carried out to examine the effect of the catalyst system (Table 1-1). In the presence of a catalytic amount of $[IrCl(cod)]_2$ (5.0 mol % with respect to Ir) and PPh_3 (PPh_3 : Ir = 1 : 1) in refluxing diglyme (bp 162 °C), the decarbonylation product, naphthalene (**2a**), was obtained in 92% yield (entry 1). The best decarbonylation catalyst reported so far, $RhCl_3{\cdot}3H_2O$ with dppp,[6b] also afforded the product in a high yield in refluxing diglyme (entry 2). However, the catalytic activity dropped drastically when the reaction was carried out in refluxing dioxane (bp 101 °C) (entry 3). Thus, the elevated temperature is a requisite for rhodium catalysts. In contrast, the $[IrCl(cod)]_2$–PPh_3 catalyst system showed a high catalytic activity, even in refluxing dioxane, and gave the product in 79% yield in 24 h and in 95% yield in 48 h (entries 4 and 5). As catalyst precursors, $IrCl_3{\cdot}3H_2O$, $[Ir(cod)_2]BF_4$ and $[IrCl_2Cp^*]_2$ gave the product in only low yields (entries 6–8). The phosphines P(*n*-Bu)$_3$ and PCy_3, of higher basicity, were more efficient and afforded the

product in 95 and 89% yields, respectively (entries 9 and 10, *cf.* entry 4), for 24 h. Although bidentate phosphines such as dppe, dppp and *rac*-BINAP were found to be noticeably effective in the Rh catalyst system,[6b–d] they were not as efficient as PPh_3 with the iridium catalyst (entries 11–13). These results suggest that the use of a monodentate phosphine is more favorable in iridium-catalyzed decarbonylation reactions. However, with excess PPh_3 (PPh_3 : Ir = 2 : 1), the yield decreased to 4% under otherwise identical conditions to those in Table 1-1, entry 4. Furthermore, the iridium catalyst system with P(*n*-Bu)$_3$ showed a good catalytic activity, even in refluxing DME (bp 85 °C) (entry 14), although PPh_3 was not such an efficient ligand in DME (entry 15). Hydrocarbon

Table 1-1. The iridium-catalyzed decarbonylation of 2-naphthaldehyde (**1a**): effect of catalyst precursors, ligands and solvents.[a]



1a **2a**

entry	[M]	ligand	solvent	time/h	**2a** % yield[b]
1	$[IrCl(cod)]_2$	PPh_3	diglyme	6	92
2[c]	$RhCl_3{\cdot}3H_2O$	dppp	diglyme	24	90
3[c]	$RhCl_3{\cdot}3H_2O$	dppp	dioxane	24	1
4	$[IrCl(cod)]_2$	PPh_3	dioxane	24	79
5	$[IrCl(cod)]_2$	PPh_3	dioxane	48	95 (87)[d]
6	$IrCl_3{\cdot}3H_2O$	PPh_3	dioxane	24	2
7	$[Ir(cod)_2]BF_4$	PPh_3	dioxane	24	14
8	$[IrCl_2Cp^*]_2$	PPh_3	dioxane	24	3
9	$[IrCl(cod)]_2$	P(*n*-Bu)$_3$	dioxane	24	95 (81)[d]
10	$[IrCl(cod)]_2$	PCy_3	dioxane	24	89 (82)[d]
11	$[IrCl(cod)]_2$	dppe	dioxane	24	28
12	$[IrCl(cod)]_2$	dppp	dioxane	24	7
13	$[IrCl(cod)]_2$	*rac*-BINAP	dioxane	24	49
14	$[IrCl(cod)]_2$	P(*n*-Bu)$_3$	DME	48	84
15	$[IrCl(cod)]_2$	PPh_3	DME	48	31
16	$[IrCl(cod)]_2$	PPh_3	toluene	24	86

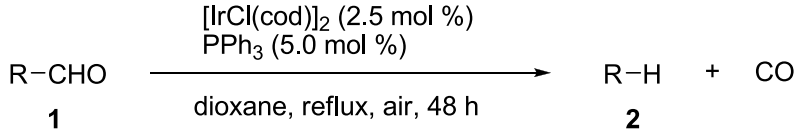
[a] Reaction conditions: 2-naphthaldehyde (0.50 mmol), [M] (0.025 mmol with respect to Ir or Rh), ligand (0.025 mmol), in refluxing solvent (1.0 mL) under Ar atmosphere. [b] GC yields. [c] dppp (0.050 mmol). [d] Under air with unpurified dioxane.

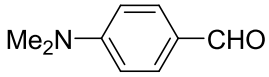
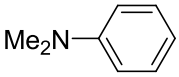
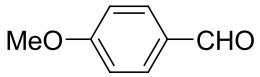
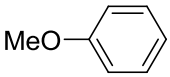
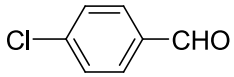
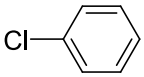
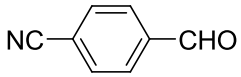
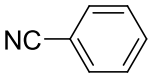
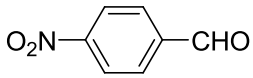
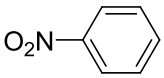
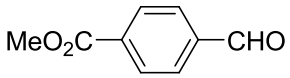
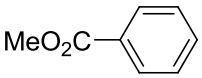
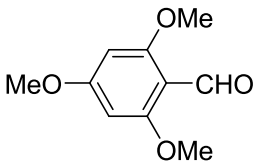
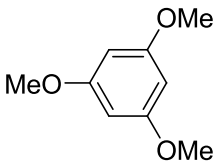
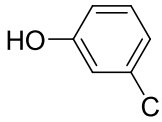
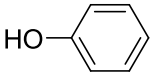
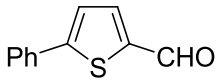
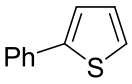
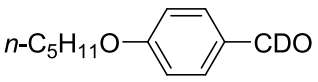
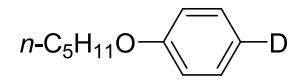
solvents, such as toluene, can also be employed in this reaction, as shown in Table 1-1, entry 16. It is noteworthy that this decarbonylation reaction can be carried out in unpurified (as received) dioxane and in air, albeit with slightly decreased yields (entries 5, 9 and 10).

The decarbonylation of aromatic aldehydes was carried out in refluxing unpurified dioxane under air (Table 1-2). Both electron-rich (entries 1 and 2) and electron-poor (entries 3–6) aldehydes provided the corresponding products in good to high yields. In the $RhCl_3 \cdot 3H_2O$–dppp catalyzed decarbonylation reaction in refluxing diglyme, 4-nitrobenzaldehyde (**1f**) was reported to be partially decomposed and afforded the decarbonylation product **2f** in only 12% yield.[6b] However, with the iridium catalyst, the decarbonylation could be carried out smoothly in refluxing dioxane, and the product was isolated in 87% yield (entry 5). A sterically hindered 2,4,6-trimethoxybenzaldehyde (**1h**) was smoothly decarbonylated (entry 7). While the decarbonylation of salicylaldehyde did not proceed, possibly due to intramolecular coordination of the OH functionality, 3-hydroxybenzaldehyde (**1i**) provided the decarbonylation product **2i** in an excellent yield (entry 8). 5-Phenylthiophene-2-carboxyaldehyde (**1j**) gave 2-phenylthiophene (**2j**) in 94% yield (entry 9), and the decarbonylation of 4-amyloxybenzaldehyde-d_1 (**1k**) afforded the product bearing the deuterium **2k** at the *para*-position in 81% yield (entry 10).

Next, Table 1-3 shows the results of the decarbonylation of various aldehydes. The decarbonylation of α,β-unsaturated aldehydes proceeded somewhat more rapidly. *trans*-Cinnamaldehyde (**1l**) provided styrene (**2l**) in 84% yield in 9 h (Table 1-3, entry 1). The product **2l** was obtained in high yield, even if the catalyst loading was reduced to one tenth of the standard amount (entry 2). In refluxing DME, **2l** was obtained in 79% yield (entry 3). When PCy_3 was used in place of PPh_3 in DME, the yield increased to 91% yield (entry 4). Surprisingly, with the $[IrCl(cod)]_2$–PCy_3 catalyst system, the decarbonylation of **1l** proceeded in high yield, even in refluxing THF (bp. 66 °C) (entry 5). The corresponding decarbonylation products were isolated in high yields from citral (**1m**) (entry 6) and (*S*)-perillaldehyde (**1n**) (entry 7). (*E*)-2-Methyl-3-phenyl-2-propenal (**1o**) afforded the decarbonylation product **2o** in 63% yield in 24 h with *E*/*Z* isomerization to *E* : *Z* = 16 : 84 (entry 8). In this case, by prolonging the reaction time to 48 h, the yield of β-methylstyrenes increased to 90%, but the isomerization proceeded further to *E* : *Z* = 93 : 7. In the case of aldehydes having β-hydrogen on the sp^3 carbon (**1p**–**r**), the decarbonylation reaction proceeded smoothly, but alkenes formed simultaneously in 5–10% yields due to β-hydride elimination (entries 9–11). As for limitations, the conversion of an α,α-dialkylated aldehyde **1s** was very low in the

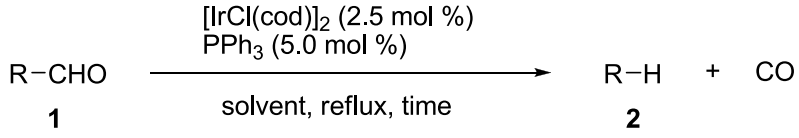
Table 1-2. The iridium-catalyzed decarbonylation of aromatic aldehydes.[a]

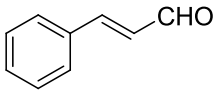
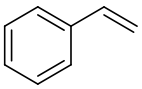
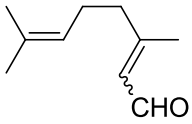
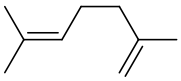
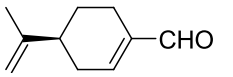
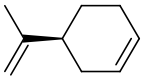
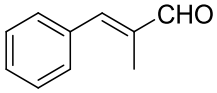
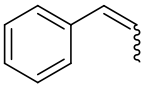
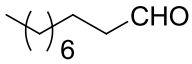
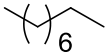
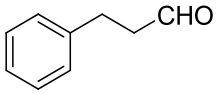
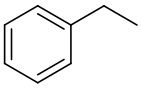
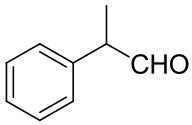
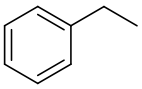
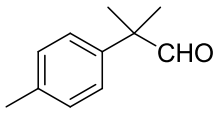
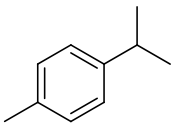


entry	aldehyde **1**		product **2**		% yield[b]
1		**1b**		**2b**	91
2		**1c**		**2c**	76
3		**1d**		**2d**	79
4		**1e**		**2e**	84
5		**1f**		**2f**	87
6		**1g**		**2g**	91
7		**1h**		**2h**	78
8		**1i**		**2i**	95[c]
9		**1j**		**2j**	94
10		**1k**		**2k**	81[d]

[a] Reaction conditions: aldehyde (1.0 mmol), $[IrCl(cod)]_2$ (0.025 mmol, 2.5 mol %), PPh_3 (0.050 mmol, 5.0 mol %), in refluxing dioxane (unpurified, 1.0 mL) for 48 h under air. [b] Isolated yields. [c] GC yield. [d] For 72 h.

Table 1-3. The iridium-catalyzed decarbonylation of various aldehydes.[a]



entry	aldehyde **1**		solvent	time/h	product **2**		% yield[b]
1		**1l**	dioxane	9		**2l**	84
2			dioxane	32			94[c,d]
3			DME	24			79[c]
4			DME	24			91[c,e]
5			THF	96			82[c,e]
6		**1m**	dioxane	24		**2m**	92
7		**1n**	dioxane	24		**2n**	82
8		**1o**	dioxane	24		**2o**	63[f]
9		**1p**	dioxane	24		**2p**	91[g]
10		**1q**	dioxane	24		**2q**	72[h]
11		**1r**	dioxane	24		**2r**	81[i]
12		**1s**	dioxane	24		**2s**	3[j]

[a] Reaction conditions: aldehyde (1.0 mmol), $[IrCl(cod)]_2$ (0.025 mmol, 2.5 mol %), PPh_3 (0.050 mmol, 5.0 mol %), in refluxing dioxane (unpurified, 1.0 mL) for 24 h under air. [b] Isolated yields. [c] Under argon. [d] $[IrCl(cod)]_2$ (0.0025 mmol, 0.25 mol %), PPh_3 (0.0050 mmol, 0.50 mol %). [e] With PCy_3 in place of PPh_3. [f] $E : Z = 16 : 84$. [g] In addition, nonenes were obtained in 5% yield. [h] In addition, styrene was obtained in 6% yield. [i] In addition, styrene was obtained in 10% yield. [j] In addition, 1-isopropenyl-4-methylbenzene was obtained in 6% yield.

present catalyst system (entry 12), as seen in previous rhodium-catalyzed reactions.[6b]

To examine the reaction mechanism of the iridium-catalyzed decarbonylation of aldehydes, the author measured the kinetic isotope effect (Figure 1-1). The rate of the iridium-catalyzed decarbonylation reaction has a first-order dependence on aldehyde concentration. Kinetic measurements with 4-amyloxybenzaldehyde-d_1 **1k** (Table 1-2, entry 10) vs. 4-methoxybenzaldehyde **1c** and a comparison of the k_D value with the k_H value for 4-amyloxybenzaldehyde-d_0 **1t** afforded a deuterium isotope effect $k_H/k_D = 1.70$. This value is comparable to $k_H/k_D = 1.77$[7a] and 1.8[7b] reported previously for rhodium-catalyzed decarbonylations. This observation indicates that the reaction mechanism for iridium-catalyzed decarbonylation would be similar to that of rhodium-catalyzed reactions.

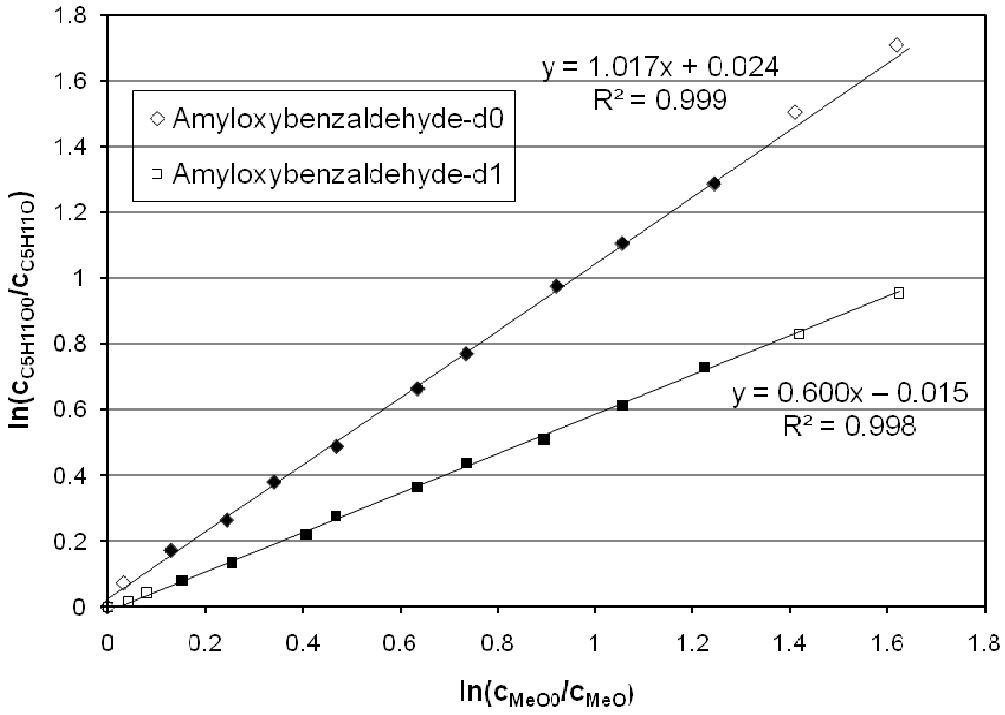
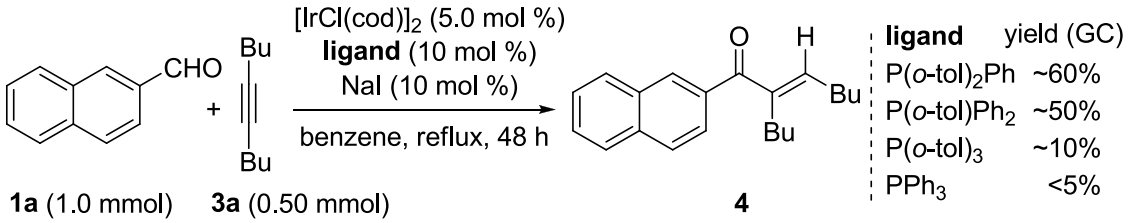


Figure 1-1. The kinetic isotope effect (k_H/k_D) measurement for the 4-amyloxybenzaldehydes.

As for preliminary results of hydroacylation, the author found that the combination of $[IrCl(cod)]_2$ and a relatively bulky monodentate phosphine such as P(*o*-tol)$_2$Ph or P(*o*-tol)Ph$_2$ was effective in the reaction of **1a** and 5-decyne (**3a**) to afford the adduct **4** in *ca.* 50–60% yields determined by GC analysis (Scheme 1-3). It is likely that the competing decarbonylation successfully is repressed under the conditions because the

moderate steric hindrance of the phosphines would stabilize the acyl-intermediate and accelerate the reductive elimination step. When bulkier P(*o*-tol)$_3$ or less bulky PPh_3 was used, the yield of **4** decreased drastically. Although this strategy might be an attractive for direct hydroacylation without external carbon monoxide and directing groups, there are some problems about the reproducibility.



Scheme 1-3. Iridium-catalyzed hydroacylation of 5-decyne with 2-naphthaldehyde.

1-3. Conclusion

In summary, the iridium-catalyzed decarbonylation of aldehydes using a catalytic amount of commercially available [IrCl(cod)]$_2$ and an easily accessible monodentate phosphine such as PPh_3 and P(*n*-Bu)$_3$ was developed. The reaction proceeded smoothly under mild reaction conditions. This practical and reliable method should be widely applicable to various substrates with excellent functional-group compatibility.

1-4. Experimental Section

Instrumentation and chemicals

The reactions in Table 1-1 were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. Reagents and solvents were dried and purified by usual procedures.[13] [IrCl(cod)]$_2$,[14] [Ir(cod)$_2$]BF_4,[15] [$IrCl_2Cp^*$]$_2$[16] and 2-methyl-2-(4-methylphenyl)propanal (**1s**)[17] were prepared as described in their literatures. 4-Amyloxybenzaldehyde-d_1 was purchased from CDN isotopes Inc. and distilled under Ar. Other chemicals were purchased from commercial sources. ^{1}H and ^{13}C NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^{1}H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm) or residual protiated solvent (7.26 ppm) in $CDCl_3$. The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). EI-MS were recorded on a Shimadzu GCMS-QP5050A with a direct inlet. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). GC analysis was carried out using Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m).

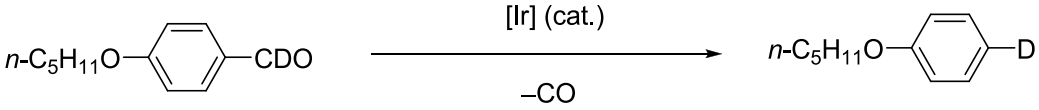
General procedures in Table 1-1

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and PPh_3 (6.6 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed dioxane (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. 2-Naphthaldehyde (**1a**, 78.1 mg, 0.50 mmol) was added to the flask and the mixture was heated under reflux (bath temp. 110 °C) for 48 h under an argon atmosphere (balloon). After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and added tridecane (0.205 mmol) as an internal standard. The yield of the product, naphthalene **2a**, was determined by GC analysis (95%).

General procedures in Table 1-2 and 1-3

$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and PPh_3 (13.1 mg, 0.050 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. Then dioxane (unpurified, 1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min in air. 4-Dimethylaminobenzaldehyde (**1b**, 149 mg, 1.0 mmol) was added to the flask and the reaction was carried out under reflux (bath temp. 110 °C) for 48 h. After cooling to room temperature, the mixture was diluted with pentane, and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated carefully. The crude product was purified by silica gel column chromatography using pentane–CH_2Cl_2 (5 : 1) as an eluent to give *N*,*N*-dimethylaniline (**2b**, 110 mg, 91%) as a colorless oil.

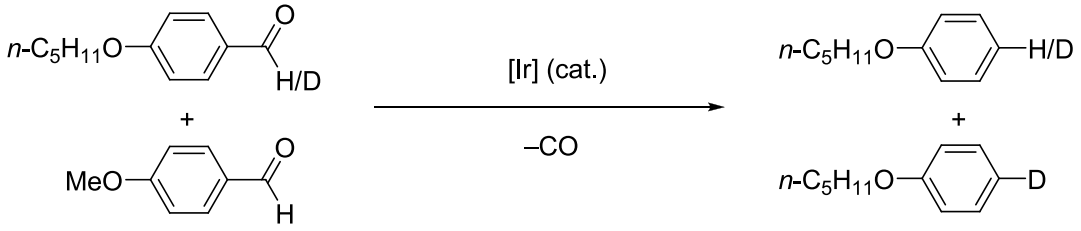
Decarbonylation of 4-amyloxybenzaldehyde-d_1 (Table 1-2, entry 10)



$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and PPh_3 (13.1 mg, 0.050 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. Then dioxane (unpurified, 1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min under an air. 4-Amyloxybenzaldehyde-d_1 (**1k**, 193 mg, 1.0 mmol, 99.7%-*d*) was added to the flask and the mixture was heated under reflux (bath temp. 110 °C) for 72 h. After cooling to room temperature, the mixture was diluted with pentane and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated carefully. The crude product was purified by silica gel column chromatography using pentane as an eluent to give 4-amyloxybenzene-d_1 (**2k**, 134 mg, 81%, deuterium incorporation >99% determined by ^1H NMR) as a colorless oil: ^1H NMR (400 MHz,

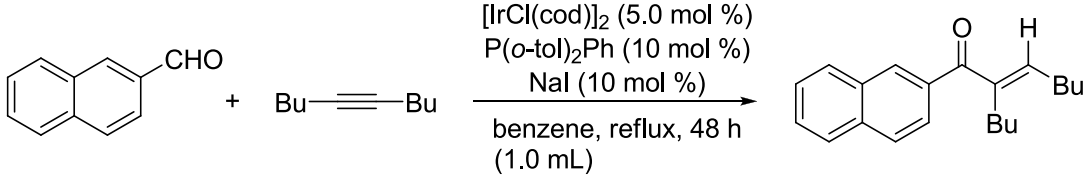
$CDCl_3$): δ 7.25 (d, J = 8.2 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 3.92 (t, J = 6.6 Hz, 2H), 1.73-1.80 (quintet, J = 7.2 Hz, 2H), 1.32-1.47 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 129.2, 120.1 ($^1J_{C\text{-}D}$ = 24 Hz), 114.4, 67.8, 29.0, 28.2, 22.5, 14.0. EI-MS: *m/z* 166 ($[M+H]^+$, 1%), 165 ($[M]^+$, 8), 95 (100).

General procedure for kinetic study (Figure 1-1)



$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and PPh_3 (13.1 mg, 0.050 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed dioxane (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. 4-Amyloxybenzaldehyde-d_0 or 4-amyloxybenzaldehyde-d_1 (1.0 mmol), 4-methoxybenzaldehyde (1.0 mmol) and bibenzyl (0.50 mmol) as an internal standard were added to the flask and the mixture was heated under reflux (bath temp. 110 °C) under an argon atmosphere (balloon). A small aliquot (0.01 mL) was taken out from the reaction mixture at suitable interval. The samples were diluted with diethyl ether (0.05 mL) and analyzed by GC (Figure 1-1). The data during 4–20 h (the conversions after 20 h were 72% for 4-amyloxybenzaldehyde-d_0 and 52% for 4-amyloxybenzaldehyde-d_1) were used for the kinetic measurement because these reactions had the induction periods.

Iridium-catalyzed hydroacylation of 3a with 1a in Scheme 1-3



1a (1.0 mmol) **3a** (0.50 mmol) **4**

$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and P(o-tol)$_2$Ph (14.5 mg, 0.050 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then benzene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. 2-Naphthaldehyde (**1a**, 156 mg, 1.0 mmol), 5-decyne (90 μL, 0.50 mmol) and NaI (7.5 mg, 0.050 mmol) were

added to the flask and the mixture was heated under reflux (bath temp. 90 °C) for 48 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and added tridecane (0.205 mmol) as an internal standard. The yield of the product **4** was determined by GC analysis (~60%).

1-5. References and Notes

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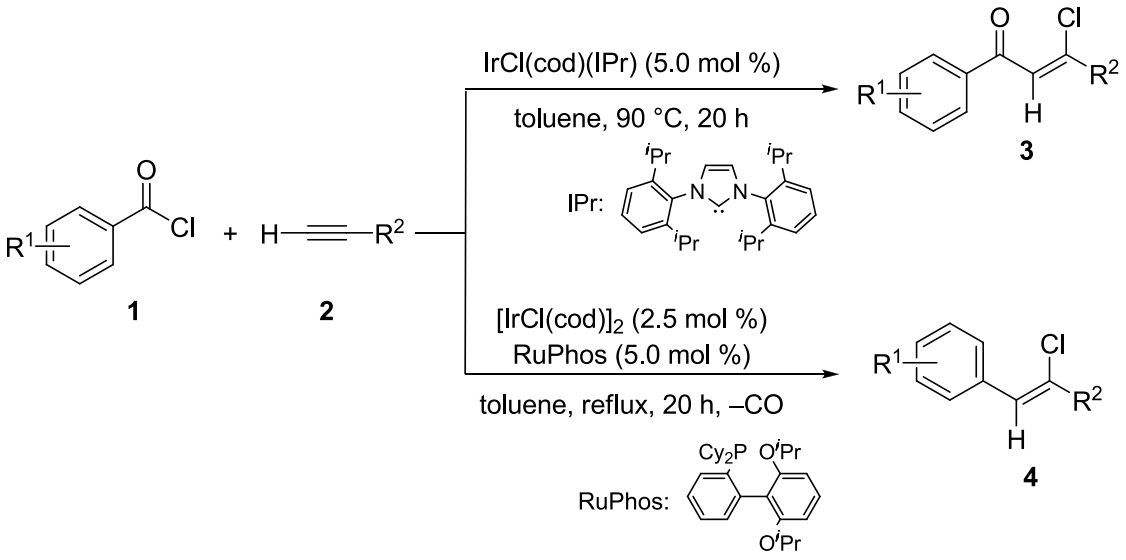
Chapter 2

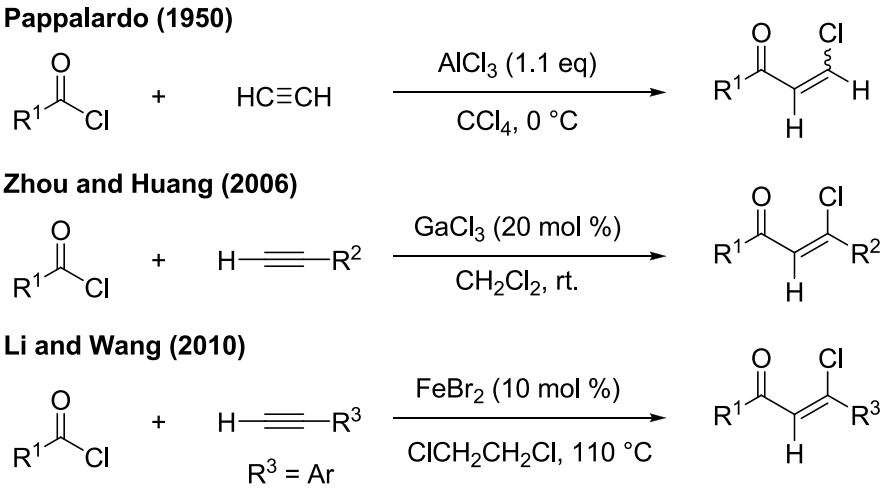
Ligand-Controlled Addition of Aromatic Acid Chlorides to Terminal Alkynes Catalyzed by Iridium Complexes

An iridium *N*-heterocyclic carbene (NHC) complex, IrCl(cod)(IPr), successfully catalyzed an addition of common aromatic acid chlorides to terminal alkynes to afford (*Z*)-*β*-chloro-*α*,*β*-unsaturated ketones regio- and stereoselectively. By changing the NHC (IPr) ligand to a phosphine (RuPhos), the addition occurred with the decarbonylation to give the corresponding (*Z*)-vinyl chlorides. Furthermore, the former reaction using IrCl(cod)(IPr) can be applied to a catalytic synthesis of 2,5-disubstituted furans.



2-1. Introduction

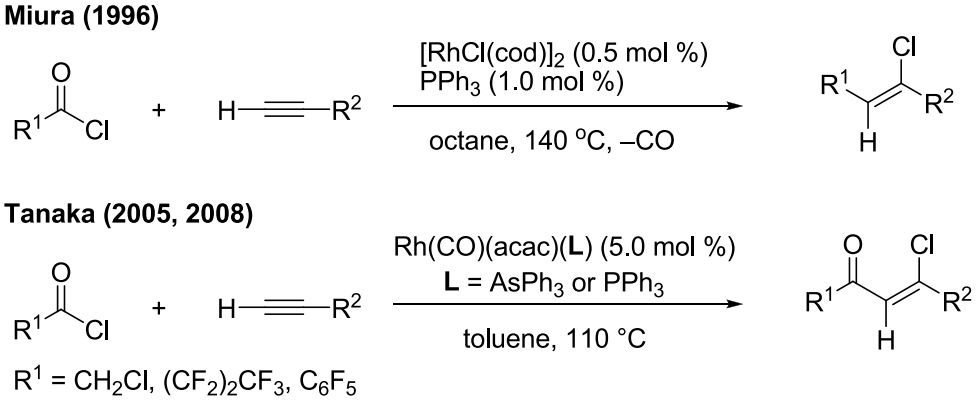
The addition of acid chlorides to alkynes should be very useful, since both the carbonyl and the chloro functionalities can be introduced simultaneously and atom-economically. The products, *β*-chloro-*α*,*β*-unsaturated ketones, are versatile intermediates in many synthetic reactions.[1] Therefore, these reactions have attracted considerable interest in the past. Since early times, the Friedel-Crafts addition of acid chlorides to alkynes using a stoichiometric[2a-c] or catalytic (20 mol %)[2d] amount of a Lewis acid such as $AlCl_3$ and $GaCl_3$ is known but suffers from low stereoselectivity of products (Scheme 2-1). Recently, iron-catalyzed addition of acid chlorides to aromatic terminal alkynes for regio- and stereoselective synthesis of *β*-chloro-*α*,*β*-unsaturated ketones has been reported.[3] However, narrow substrate scope and low stereoselectivity of these methods has limited their synthetic application. Therefore, a capable catalyst system must be developed for the reaction.



Scheme 2-1. Lewis acid-mediated or -catalyzed addition of acid chlorides to alkynes.

In transition-metal-catalyzed reactions, acid chlorides[4] are valuable substrates because of their facile oxidative addition to metal centers.[5] However, the carbonyl functionality is often lost during the catalysis[4a–c] via facile decarbonylation steps. In 1996, Miura, Nomura and co-workers have reported a pioneering rhodium-catalyzed addition of acid chlorides to terminal alkynes (Scheme 2-2).[6] In this case, the carbonyl functionality was also lost completely to form (*Z*)-vinyl chlorides exclusively. Recently, Tanaka and co-workers adapted the reaction by employing perfluorinated acid chlorides[7a] or chloroacetyl chlorides[7b] as restricted substrates and achieved the reaction without the decarbonylation. Thus, to date, use of acid chlorides as the substrate[8] has

severe limitations in realizing the CO-retentive addition. In this Chapter, the author discloses that an iridium *N*-heterocyclic carbene (NHC) complex successfully catalyzes the addition of common aromatic acid chlorides (**1**) to terminal alkynes (**2**) without decarbonylation regio- and stereoselectively. On the other hand, when the NHC ligand is changed to a phosphine, the addition reaction proceeds via decarbonylation.

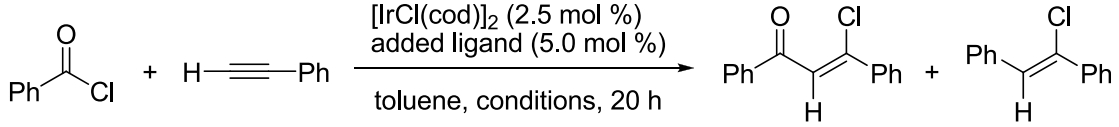


Scheme 2-2. Rhodium-catalyzed addition of acid chlorides to terminal alkynes.

2-2. Results and Discussion

For the reaction optimization, a reaction of benzoyl chloride (**1a**) and phenylacetylene (**2a**) was carried out employing various ligands with a catalytic amount of $[IrCl(cod)]_2$ in refluxing toluene (Table 2-1). By use of PCy_3, the addition of **1a** and **2a** was realized to afford the addition product (**3a**) in moderate yield (53%) with a considerable amount (12%) of the decarbonylated product (**4a**) (entry 1). With PPh_3, **3a** was afforded only in 6% yield (entry 2). Without added ligands or with *rac*-BINAP under otherwise identical reaction conditions, **3a** and **4a** were obtained in <1% (entries 3 and 4). On the other hand, NHC ligand,[9] IMes, generated *in situ* from IMes·HCl and KO^{t}Bu provided **3a** in 37% yield (entry 5). As for the NHC ligand, IPr generated from IPr·HCl and KO^{t}Bu was much more effective to afford **3a** selectively in 88% yield (entry 6). Even at 90 °C, **3a** was obtained in 80% yield regio- and stereoselectively (entry 7). By using IrCl(cod)(IPr),[10] the isolated complex bearing IPr ligand, **3a** was obtained much effectively with high (*Z*)-selectivity (91% yield, *Z*/*E* = 99/1; entry 8). In sharp contrast, Buchwald-type phosphines[11] such as SPhos and RuPhos provided decarbonylated product **4a** as a major product in 61% and 72% yields, respectively (entries 9 and 10). Thus, the ligands in the catalytic reaction play a critical role to determine the selectivity of the products.

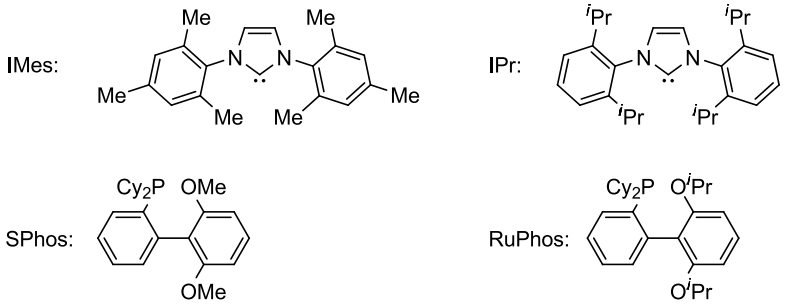
Table 2-1. Reaction optimization for the addition of benzoyl chloride (**1a**) to phenylacetylene (**2a**).[a]



1a **2a** **3a** **4a**

entry	added ligand	conditions	**3a** % yield[b] (*Z*/*E*)[c]	**4a** % yield[b]
1	PCy_3	reflux	53 (94/6)	12
2	PPh_3	reflux	6	<1
3	none	reflux	<1	<1
4	*rac*-BINAP	reflux	<1	<1
5	IMes·HCl/KO^{t}Bu	reflux	37 (87/13)	4
6	IPr·HCl/KO^{t}Bu	reflux	88 (98/2)	2
7	IPr·HCl/KO^{t}Bu	90 °C	80 (98/2)	<1
8	IrCl(cod)(IPr)[d]	90 °C	91[e] (99/1)	<1
9	SPhos	reflux	12	61
10	RuPhos	reflux	9	72 (70)[e]

[a] Benzoyl chloride (0.50 mmol), phenylacetylene (0.75 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), added ligand (0.025 mmol, 5.0 mol %), toluene (1.0 mL), 20 h. [b] Yields were determined by GC analysis. [c] *Z*/*E* ratio were determined by GC analysis. [d] IrCl(cod)(IPr) (0.025 mmol, 5.0 mol %) was used as for the catalyst. [e] Isolated yields.



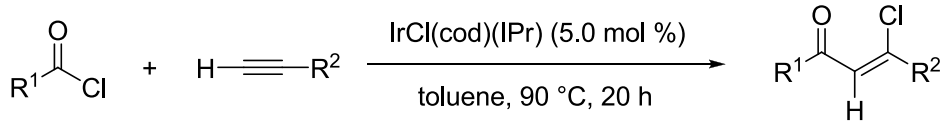
Various *β*-chloro-*α*,*β*-unsaturated ketones (**3**) were obtained regio- and stereoselectively from **1** and **2** in the presence of catalytic amount of IrCl(cod)(IPr) (Table 2-2). Electron-rich (**1b** and **1c**) and electron-poor (**1d**–**f**) aroyl chlorides were smoothly converted to **3b**–**f** in high yields without decarbonylation (entries 1–5). The regio- and stereochemistry of all products were unambiguously determined with the aid of 2D NMR spectroscopy. The *Z* configuration of **3e** and **3f** was further confirmed by a single-crystal X-ray diffraction study. 2-Thenoyl chloride (**1g**) afforded the

corresponding ketone **3g** in high yield (entry 6). The reaction of a terephthaloyl chloride (**1h**) with two equivalent of **2a** gave pure **3h** in good yield (entry 7). Various terminal alkynes, including enyne **2e** and 1-decyne (**2f**), afforded the corresponding **3i**–**m** regioselectively (entries 8–12). Neither *α*,*β*-unsaturated acid chlorides, aliphatic acid chlorides, nor internal alkynes provided **3**.

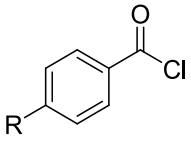
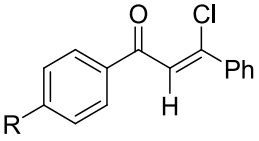
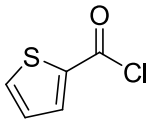
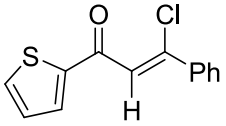
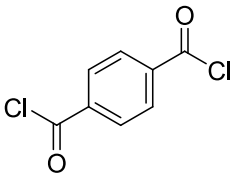
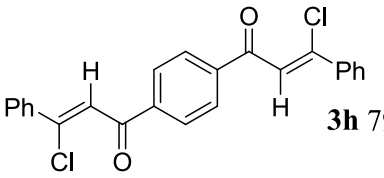
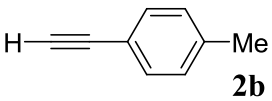
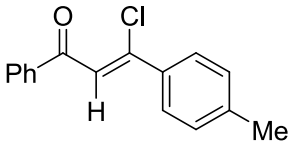
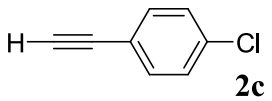
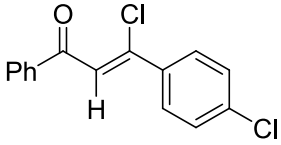
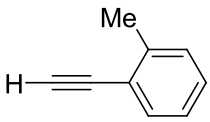
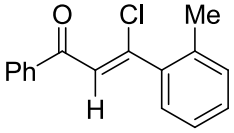
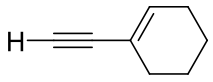
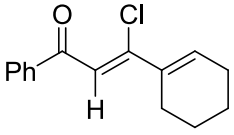
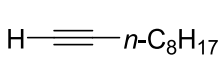
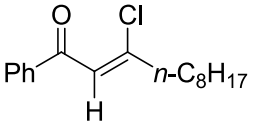
When the reaction of **2f** (Table 2-2, entry 12) was carried out at higher temperature (in refluxing toluene) under otherwise identical reaction conditions, **3m** was not obtained; instead, 2-heptyl-5-phenylfuran (**5a**) was produced in good yield (Table 2-3). Employing isolated **3m** as a substrate afforded **5a** in 86% yield under similar conditions (5.0 mol % IrCl(cod)(IPr), *o*-xylene, 120 °C, 20 h). This observation unambiguously indicated that **5a** was produced via **3m**. As shown in Table 2-3, terminal alkynes bearing a methylene unit adjacent to the triple bond afforded the corresponding 2,5-disubstituted furans (**5b**–**g**) in moderate to high yields at elevated temperatures. To the best of his knowledge, the present reaction is the first example of a catalytic furan synthesis from acid chlorides and alkynes.[12,13]

In contrast, as mentioned above in Table 2-1, when the NHC ligand (IPr) was changed to a phosphine ligand (RuPhos), the addition occurred with decarbonylation to afford the corresponding (*Z*)-vinyl chlorides **4a**–**j** in good-to-high isolated yields as the pure forms (Table 2-4). Thus, the ligands in the catalytic reaction play a critical role in distinguishing the products **3** and **4**.

Table 2-2. Addition of acid chlorides **1** to terminal alkynes **2**.[a]

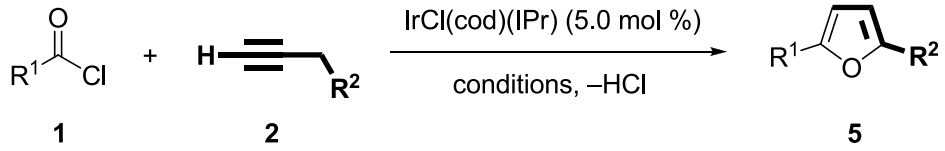


1 **2** **3**

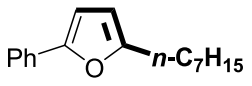
entry	**1**		**2**	**3**	% yield[b] (*Z*/*E*)[c]
1		R = Me **1b**			**3b** 91 (99/1)
2		R = OMe **1c**			**3c** 89 (98/2)
3		R = Cl **1d**	**2a**		**3d** 94 (99/1)
4		R = CF_3 **1e**			**3e** 92 (99/1)
5[d]		R = CO_2Me **1f**			**3f** 87 (93/7)
6		**1g**	**2a**		**3g** 94 (>99/1)
7[e]		**1h**	**2a**		**3h** 79 (100/0)
8	**1a**		**2b**		**3i** 92 (99/1)
9	**1a**		**2c**		**3j** 59 (>99/1)
10[f]	**1a**		**2d**		**3k** 85 (>99/1)
11	**1a**		**2e**		**3l** 90 (99/1)
12[f]	**1a**		**2f**		**3m** 70 (82/18)

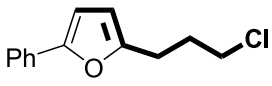
[a] Conditions: acid chloride (0.50 mmol), alkyne (0.75 mmol), IrCl(cod)(IPr) (0.025 mmol, 5.0 mol %), toluene (1.0 mL), 90 °C, 20 h. [b] Isolated yields. [c] Determined by GC analysis. [d] Using a reaction time of 36 h. [e] Using 1.5 mmol of **2a**. [f] Using a reaction time of 48 h.

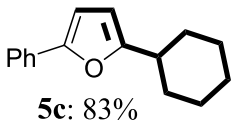
Table 2-3. Iridium-catalyzed synthesis of furans **5**.[a]

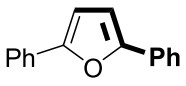


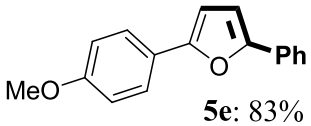
1 **2** **5**

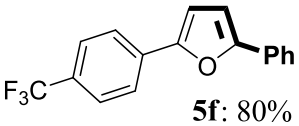

5a: 75% (toluene, reflux, 48 h)

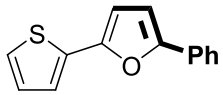

5b: 64% (xylene, 120 °C, 24 h)


5c: 83% (xylene, 120 °C, 20 h)


5d: 79% (xylene, 120 °C, 20 h)

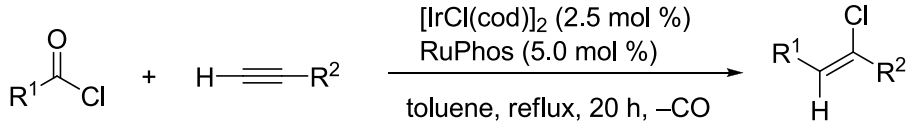

5e: 83% (toluene, reflux, 30 h)


5f: 80% (xylene, 120 °C, 20 h)


5g: 39% (xylene, 120 °C, 24 h)

[a] Conditions: acid chloride (0.50 mmol), alkyne (0.75 mmol), IrCl(cod)(IPr) (0.025 mmol, 5.0 mol %), solvent (1.0 mL). Isolated yields of **5** are shown.

Table 2-4. Decarbonylative addition of **1** to **2**.[a]

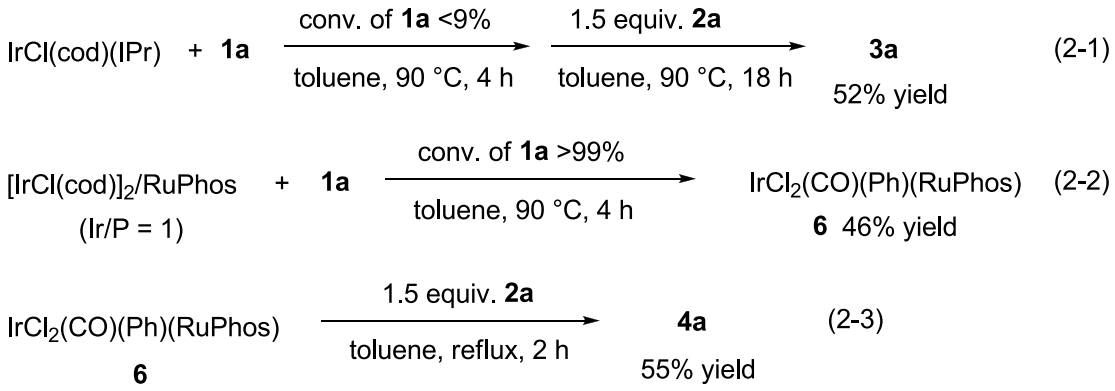


1 **2** **4**

entry	**1**: R^1	**2**: R^2	**4**	% yield[b]
1	**1b**: 4-MeC_6H_4	**2a**: Ph	**4b**	84
2	**1c**: 4-$MeOC_6H_4$	**2a**: Ph	**4c**	49
3	**1d**: 4-ClC_6H_4	**2a**: Ph	**4d**	69
4	**1g**: 2-thienyl	**2a**: Ph	**4e**	82
5	**1i**: 2-furyl	**2a**: Ph	**4f**	58
6	**1j**: (*E*)-C_6H_5CH=CH	**2a**: Ph	**4g**	88
7	**1a**: Ph	**2e**: 1-cyclohexenyl	**4h**	43
8	**1a**: Ph	**2g**: Cy	**4i**	73
9	**1a**: Ph	**2h**: *n*-C_6H_{13}	**4j**	81

[a] Conditions: acid chloride (0.50 mmol), alkyne (0.75 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), RuPhos (0.025 mmol, 5.0 mol %), toluene (1.0 mL), reflux, 20 h. [b] Isolated yields.

To gain further insight into the mechanisms, reactions of an acid chloride with the two catalyst precursors, IrCl(cod)(IPr) and $[IrCl(cod)]_2$/RuPhos, respectively, were carried out. Surprisingly, in a stoichiometric reaction of IrCl(cod)(IPr) with **1a**, most of the **1a** (>91% by GC) remained intact, even at 90 °C for 4 h. However, when **2a** was further added into the reaction system, most of **1a** was converted and **3a** was obtained in 52% yield (eq 2-1): Thus, in eq 2-1 (Table 2-2), **2** may first coordinate to the iridium center, after which oxidative addition of **1** followed by a fast insertion of **2** would afford **3** without decarbonylation. On the other hand, a stoichiometric reaction of $[IrCl(cod)]_2$/RuPhos (1:1 = Ir/P) with **1a** resulted in complete conversion of **1a** and provided the complex $IrCl_2(CO)(Ph)(RuPhos)$ (**6**), as confirmed by an X-ray diffraction study, in 46% yield via decarbonylation (eq 2-2, Figure 2-1). Treatment of **6** with **2a** in refluxing toluene for 2 h afforded **4a** in 55% yield (eq 2-3). Hence, in eq 2-2 (Table 2-4), oxidative addition of **1** followed by a fast decarbonylation and a successive insertion of **2** might afford **4** as the product. These quite different reactivities of the two catalyst precursors toward acid chlorides must be crucial in the catalysis.



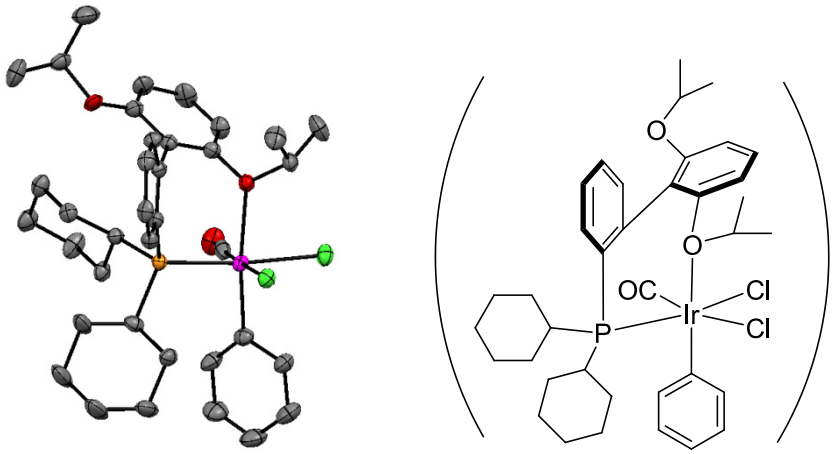


Figure 2-1. Crystal structure of **6**.

A plausible catalytic cycle in the case of IrCl(cod)(IPr) was shown in Scheme 2-3. An alkyne (**2**) may first coordinate to the iridium center giving **B** (step 1), then oxidative addition of acid chloride (**1**) followed by an insertion of the alkyne (**2**) into the Ir–Cl bond of **C** would occur to generate **D** (steps 2 and 3).[6,7,14] Finally, C-C reductive elimination would afford the desired product (**3**) and the iridium catalyst **A** regenerates (step 4). In addition, by use of terminal alkynes bearing a methylene unit adjacent to the triple bond ($R^2 = CH_2R^3$), furan derivative (**5**) was provided under the elevated temperature along with the elimination of HCl followd by intramolecular cyclization and isomerization from an allene derivatives **E** as a putative intermediate.[12]

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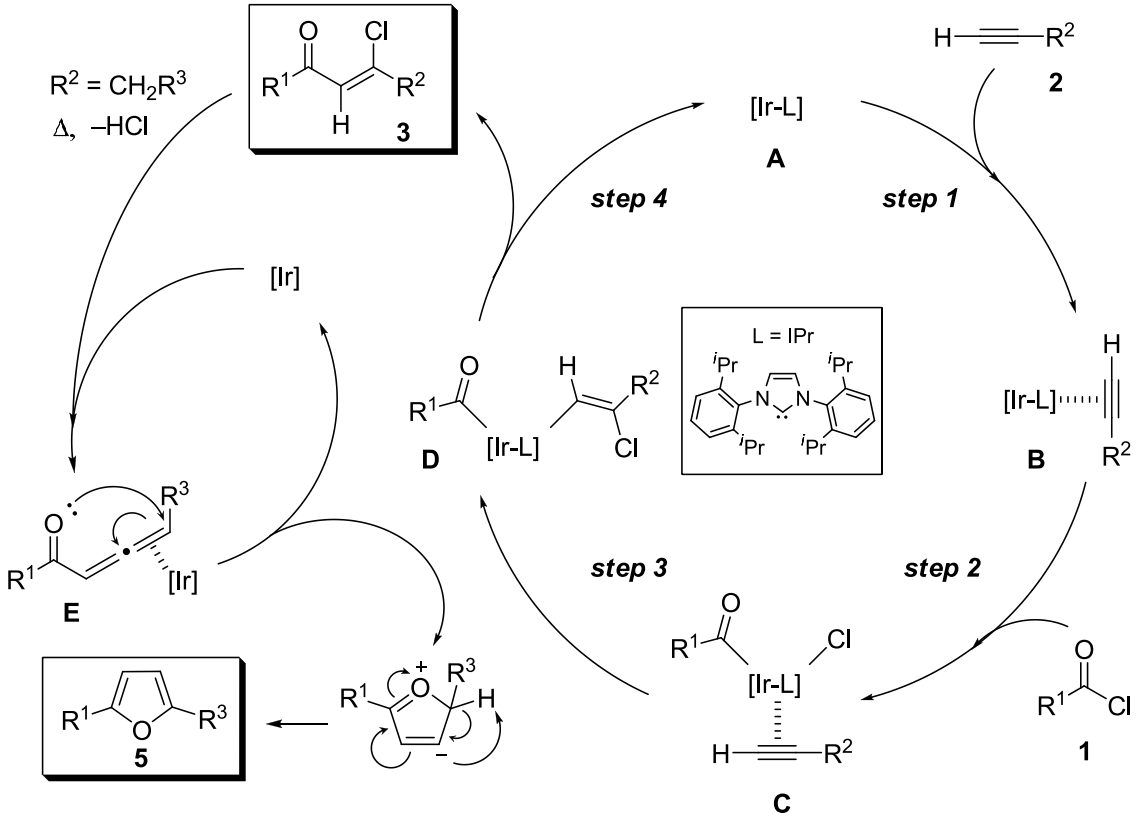


Scheme 2-3. A plausible catalytic cycle for the iridium-catalyzed addition of acid chlorides to terminal alkynes.

2-3. Conclusion

In summary, (*Z*)-*β*-chloro-*α*,*β*-unsaturated ketones (**3**) or (*Z*)-vinyl chlorides (**4**) were selectively obtained by the iridium-catalyzed addition of acid chlorides (**1**) to terminal alkynes (**2**) upon the proper choice of the IPr or RuPhos ligand. The synthesis of **3** was applied to the preparation of 2,5-disubstituted furans (**5**).

2-4. Experimental Section

Instrumentation and chemicals

All manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. All solvents were dried and purified by usual procedures.[15] Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. RuPhos and SPhos were purchased from Aldrich. *N*-Heterocyclic carbenes (IPr and IMes),[16] $[IrCl(cod)]_2$,[17] and IrCl(cod)(IPr)[10] were prepared according to literatures. IR spectra were obtained on SHIMADZU FTIR-8300 spectrometer. ^1H, ^{13}C and ^{31}P NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^1H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). The ^{31}P NMR chemical shifts are reported relative to 85% H_3PO_4 (0.00 ppm) as an external standard. EI-MS were recorded on a Shimadzu GCMS-QP5050A with a direct inlet. MALDI-TOF-MS spectra were recorded on a Bruker Autoflex. High-resolution mass spectrum (FAB-HRMS) was obtained with JEOL JMX-SX 102A spectrometer. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). Melting points were measured on a Yanako MP-J3 apparatus. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$.

General procedures in Table 2-1

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and the added ligand (0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1a** (58 μL, 0.50 mmol) and **2a** (83 μL, 0.75 mmol) were added to the flask and the mixture was heated under reflux (bath temp. 120 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and added tridecane (50 μL, 0.205 mmol) as an internal standard. The yields and *Z/E* ratio of the products, **3a** and **4a**, were determined by GC analysis.

General procedures in Table 2-2

IrCl(cod)(IPr) (18.1 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask. An acid chloride (**1**) (0.50 mmol) and a terminal alkyne (**2**) (0.75 mmol) were added to the flask and the mixture was stirred at 90 °C for 20 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the addition product was isolated by silica gel column chromatography.

General procedures in Table 2-3

IrCl(cod)(IPr) (18.1 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask. An acid chloride (**1**) (0.50 mmol) and a terminal alkyne (**2**) (0.75 mmol) were added to the flask and the mixture was stirred under reflux (bath temp 120 °C) for 20 h under an argon flow. After cooling to room temperature, the mixture was evaporated and the addition product was isolated by silica gel column chromatography.

General procedures in Table 2-4

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and RuPhos (11.6 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. An acid chloride (**1**) (0.50 mmol) and a terminal alkyne (**2**) were added to the flask and the mixture was stirred under reflux (bath temp. 120 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the addition product was isolated by silica gel column chromatography.

Procedure in eq 2-1

IrCl(cod)(IPr) (36.2 mg, 0.050 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1a** (5.8 μL, 0.050 mmol) and tridecane (25 μL, 0.1025 mmol) as an internal standard were added to the flask and the mixture was heated at 90 °C for 4 h under an argon atmosphere. A small aliquot (0.01 mL) was taken out from the reaction mixture and the samples were diluted with diethyl ether (0.02 mL)

and analyzed by GC. Subsequently, to the reaction mixture was added **2a** (8.2 μL, 0.075 mmol) and stirred at 90 °C for 18 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (2.0 ml) and the yield of **3a** was determined by GC analysis.

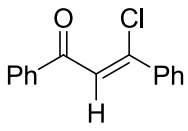
Procedures in eqs 2-2 and 2-3

$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and RuPhos (23.3 mg, 0.050 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1a** (5.8 μL, 0.050 mmol) and tridecane (25 μL, 0.1025 mmol) as an internal standard were added to the flask and the mixture was heated at 90 °C for 4 h under an argon atmosphere. A small aliquot (0.01 mL) was taken out from the reaction mixture and the samples were diluted with diethyl ether (0.02 mL) and analyzed by GC. After cooling to room temperature, the mixture was evaporated and the crude product was washed with diethyl ether (0.5 mL x 3) to give off-white solids of $IrCl_2(CO)(Ph)(RuPhos)$ (**6**) (19.3 mg, 46% yield). Further purification was done by recrystallization from CH_2Cl_2/hexane solution.

The iridium complex **6** (41.7 mg, 0.050 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **2a** (8.2 μL, 0.075 mmol) and tridecane (25 μL, 0.1025 mmol) as an internal standard were added to the flask and the mixture was heated under reflux (bath temp. 120 °C) for 2 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (2.0 ml) and the yield of **4a** was determined by GC analysis.

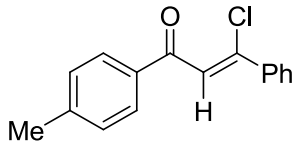
Characterization of the Compounds

(*Z*)-3-Chloro-1,3-diphenyl-2-propen-1-one (**3a**)[18]



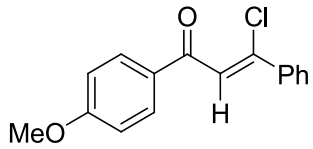
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1) and identified by ^1H, ^{13}C NMR and MS spectra according to the reported data. Pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$): δ 7.97-8.02 (m, 2H), 7.72-7.80 (m, 2H), 7.55-7.62 (m, 1H), 7.39-7.52 (m, 5H), 7.35 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.8, 143.3, 137.7, 137.3, 133.3, 130.5, 128.68, 128.65, 128.62, 127.1, 121.5. EI-MS: *m/z* 244 (17%, $[M+2]^+$), 243 (40, $[M+1]^+$), 242 (49, $[M]^+$), 241 (100, $[M-1]^+$), 165 (29), 105 (56), 77 (62).

(*Z*)-3-Chloro-1-(4-methylphenyl)-3-phenyl-2-propen-1-one (**3b**)



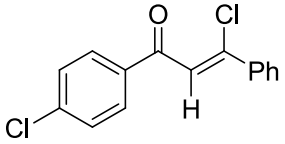
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow solids: m.p. 67-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 8.2 Hz, 2H), 7.75 (dd, J = 8.9, 1.8 Hz, 2H), 7.41-7.46 (m, 3H), 7.31 (s, 1H), 7.28 (d, J = 8.2 Hz, 2H). 2.41 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.5. 144.3, 142.6, 137.3, 135.1, 130.4, 129.4, 128.8, 128.6, 127.1, 121.7, 21.7. IR (KBr): 1652.9, 1608.5, 1585.4, 1575.7, 1238.2, 763.8 cm^{-1}. EI-MS: *m/z* 258 (17%, $[M+2]^+$), 257 (38, $[M+1]^+$), 256 (46, $[M]^+$), 255 (100, $[M-1]^+$), 221 (6, $[M-Cl]^+$), 119 (59), 91 (57). Anal. Calcd. for $C_{16}H_{13}ClO$: C, 74.85; H, 5.10. Found: C, 75.03; H, 5.12.

(*Z*)-3-Chloro-1-(4-methoxylphenyl)-3-phenyl-2-propen-1-one (**3c**)



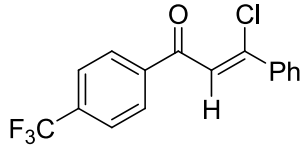
Isolated by column chromatography (silica gel, hexane/AcOEt = 8/1). Pale yellow solids: m.p. 88-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.6 Hz, 2H), 7.77 (dd, J = 7.7, 3.6 Hz, 2H), 7.40-7.45 (m, 3H), 7.28 (s, 1H), 6.95 (d, J = 8.6 Hz, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.6, 163.8, 141.8, 137.2, 131.0, 130.4, 130.3, 128.6, 127.0, 121.9, 113.8, 55.4. IR (KBr): 1651.0, 1602.7, 1585.4, 1573.8, 1242.1 cm^{-1}. EI-MS: *m/z* 274 (17%, $[M+2]^+$), 273 (31, $[M+1]^+$), 272 (51, $[M]^+$), 271 (100, $[M-1]^+$), 165 (27), 135 (100), 77 (47). Anal. Calcd. for $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80. Found: C, 70.55; H, 4.98.

(*Z*)-3-Chloro-1-(4-chlorolphenyl)-3-phenyl-2-propen-1-one (**3d**)



Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow solids: m.p. 66-67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.6 Hz, 2H), 7.74 (dd, J = 6.2, 2.7 Hz, 2H), 7.40-7.50 (m, 5H), 7.25 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.5, 143.8, 139.7, 137.0, 136.0, 130.7, 130.0, 129.0, 128.7, 127.1, 120.8. IR (KBr): 1662.5, 1587.3, 1573.8, 1203.5, 761.8 cm^{-1}. EI-MS: *m/z* 278 (14%, $[M+2]^+$), 277 (67, $[M+1]^+$), 276 (42, $[M]^+$), 275 (100, $[M-1]^+$), 165 (29), 139 (53), 102 (57), 75 (46). Anal. Calcd. for $C_{15}H_{10}Cl_2O$: C, 65.01; H, 3.64. Found: C, 65.20; H, 3.66.

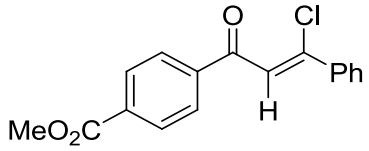
(*Z*)-3-Chloro-1-(4-trifluoromethylphenyl)-3-phenyl-2-propen-1-one (**3e**)



Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 3/1). White solids: m.p. 79-80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.2 Hz, 2H),

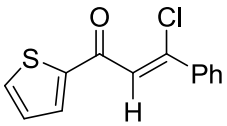
7.73-7.81 (m, 4H), 7.42-7.52 (m, 3H), 7.35 (s, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 188.6, 145.0, 140.1, 137.0, 134.3 (q, $^{2}J_{C\text{-}F}$ = 33.4 Hz), 130.9, 128.8, 128.7, 127.2, 125.7 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 123.5 (q, $^{1}J_{C\text{-}F}$ = 272.8 Hz), 120.5. IR (KBr): 1660.6, 1593.2, 1577.7, 1319.2, 1153.4, 1014.5 cm^{-1}. EI-MS: *m/z* 312 (16%, $[M+2]^+$), 311 (39, $[M+1]^+$), 310 (50, $[M]^+$), 309 (100, $[M-1]^+$), 275 (4, $[M-Cl]^+$), 165 (27), 145 (44), 102 (42). Anal. Calcd. for $C_{16}H_{10}ClF_3O$: C, 61.85; H, 3.24. Found: C, 61.68; H, 3.26.

(*Z*)-4-(3-Chloro-1-oxo-3-phenyl-2-propenyl)benzoic acid methyl ester (**3f**)



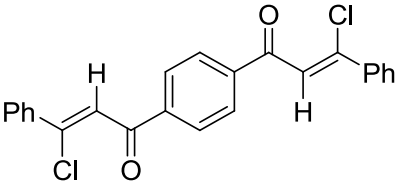
Isolated by column chromatography (silica gel, hexane/AcOEt = 6/1). Pale yellow solids: m.p. 84-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.2 Hz, 2H), 8.03 (d, *J* = 8.2 Hz, 2H), 7.76 (dd, *J* = 8.2, 2.3 Hz, 2H), 7.42-7.48 (m, 3H), 7.37 (s, 1H), 3.95 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 189.0, 166.1, 144.6, 141.1 137.0, 133.9, 130.8, 129.8, 128.7, 128.4, 127.2, 120.7, 52.4. IR (KBr): 1718.5, 1664.5, 1569.9, 1276.8, 1107.1 cm^{-1}. EI-MS: *m/z* 302 (17%, $[M+2]^+$), 301 (40, $[M+1]^+$), 300 (51, $[M]^+$), 299 (100, $[M-1]^+$), 269 (8), 165 (30), 135 (21). Anal. Calcd. for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36. Found: C, 67.68; H, 4.45.

(*Z*)-3-Chloro-3-phenyl-1-(2-thienyl)-2-propen-1-one (**3g**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow-brown oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.79 (m, 3H), 7.67 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.42-7.47 (m, 3H), 7.35 (s, 1H), 7.14 (dd, *J* = 5.0, 4.1 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 181.0, 145.5, 144.4, 137.3, 134.3, 132.0, 130.7, 128.6, 128.2, 127.2, 120.3. IR (neat): 1645.2, 1575.7, 1558.4, 1446.5, 1245.9 cm^{-1}. EI-MS: *m/z* 250 (17%, $[M+2]^+$), 249 (41, $[M+1]^+$), 248 (46, $[M]^+$), 247 (100, $[M-1]^+$), 213 (9, $[M-Cl]^+$), 184 (19), 165 (12), 111 (85). Anal. Calcd. for $C_{13}H_9ClOS$: C, 62.79; H, 3.65. Found: C, 62.98; H, 3.81.

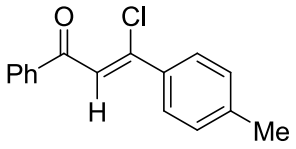
(*Z*,*Z*)-1,1'-(1,4-Phenylene)bis(3-chloro-3-phenyl)-2-propen-1-one (**3h**)



Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 1/1). Pale yellow solids: m.p. 151-152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 4H), 7.74-7.81 (m, 4H), 7.43-7.51 (m, 6H), 7.38 (s, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 188.9, 144.8, 141.1, 137.0, 130.8, 128.8, 128.7, 127.2, 120.7. IR (KBr): 1662.5, 1593.1, 1577.7, 1205.4 cm^{-1}.

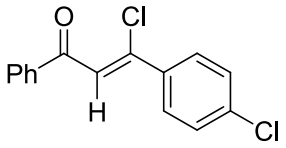
MALDI-TOF-MS (DIT): *m/z* 407 ($[M+1]^+$), 371 ($[M–Cl]^+$). Anal. Calcd. for $C_{24}H_{16}C_{l2}O_2$: C, 70.77; H, 3.96. Found: C, 70.90; H, 4.01.

(*Z*)-3-Chloro-3-(4-methylphenyl)-1-phenyl-2-propen-1-one (**3i**)



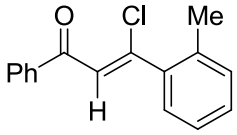
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 2H), 7.33 (s, 1H), 7.23 (d, J = 8.2 Hz, 2H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.7, 143.6, 141.0, 137.9, 134.4, 133.1, 129.3, 128.6, 128.5, 127.1, 120.3, 21.2. IR (neat): 1662.5, 1596.9, 1581.5, 1506.3, 1205.4, 1018.3, 777.3 cm^{-1}. EI-MS: *m/z* 258 (7%, $[M+2]^+$), 257 (19, $[M+1]^+$), 256 (20, $[M]^+$), 255 (53, $[M–1]^+$), 241 (100, $[M–CH_3]^+$), 179 (33), 115 (56), 105 (56). Anal. Calcd. for $C_{16}H_{13}ClO$: C, 74.85; H, 5.10. Found: C, 75.09; H, 5.25.

(*Z*)-3-Chloro-3-(4-chlorophenyl)-1-phenyl-2-propen-1-one (**3j**)



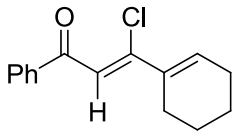
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow solids: m.p. 56-57 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.2 Hz, 2 H), 7.68 (d, J = 8.6 Hz, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.2 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.32 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.6, 141.8, 137.4, 136.6, 135.6, 133.4, 128.8, 128.7, 128.6, 128.4, 121.7. IR (KBr): 1660.6, 1598.9, 1487.0, 1091.6, 1014.5 cm^{-1}. EI-MS: *m/z* 280 (3%, $[M+4]^+$), 279 (8, $[M+3]^+$), 278 (19, $[M+2]^+$), 277 (33, $[M+1]^+$), 276 (29, $[M]^+$), 275 (46, $[M–1]^+$), 241 (29, $[M–Cl]^+$), 199 (34), 178 (31), 105 (57), 77 (100). Anal. Calcd. for $C_{15}H_{10}Cl_2O$: C, 65.01; H, 3.64. Found: C, 65.18; H, 3.76.

(*Z*)-3-Chloro-3-(2-methylphenyl)-1-phenyl-2-propen-1-one (**3k**)



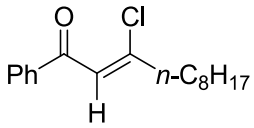
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-8.01 (m, 2H), 7.58-7.60 (m, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.37 (d, J = 7.7 Hz, 1H), 7.29-7.32 (m, 1H), 7.21-7.27 (m, 2H), 6.98 (s, 1H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.4, 143.1, 138.6, 137.4, 135.5, 133.3, 130.7, 129.5, 128.67, 128.63, 128.57, 125.9, 125.0, 19.9. IR (neat): 1668.3, 1596.9, 1213.1, 1014.5, 759.9 cm^{-1}. EI-MS: *m/z* 257 (0.7%, $[M+1]^+$), 256 (0.5, $[M]^+$), 255 (2, $[M–1]^+$), 241 (69), 220 (18), 115 (49), 105 (79), 77 (100). Anal. Calcd. for $C_{16}H_{13}ClO$: C, 74.85; H, 5.10. Found: C, 75.12; H, 5.28.

(*Z*)-3-Chloro-3-(1-cyclohexen-1-yl)-1-phenyl-2-propen-1-one (**3l**)



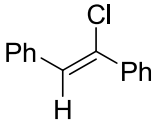
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 3/1). This compound was rather unstable under air and moisture, and turned to black gum in a few days. Pale yellow solids: m.p. 51-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.7 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 2H), 6.88 (s, 1H), 6.76 (s, 1H), 2.24-2.39 (m, 4H), 1.59-1.80 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 190.9, 143.7, 137.9, 135.3, 133.3, 133.0, 128.53, 128.49, 118.1, 26.22, 26.17, 22.4, 21.5. IR (KBr): 2933.5, 1654.8, 1664.5, 1595.0, 1566.1, 1448.4, 1226.6 cm^{-1}. EI-MS: *m/z* 248 (7%, $[M+2]^+$), 247 (9, $[M+1]^+$), 246 (21, $[M]^+$), 245 (19, $[M-1]^+$), 217 (100), 211 (98, $[M-Cl]^+$), 105 (99), 77 (76). FAB-HRMS: Calcd. for $C_{15}H_{16}ClO$ ($[M+H]^+$), 247.0890. Found, 247.0888.

(*Z*)-3-Chloro-1-phenyl-2-undecen-1-one (**3m**)



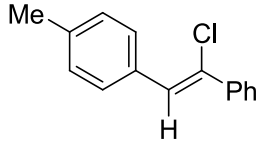
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 3/1). Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 6.82 (s, 1H), 2.53 (t, J = 7.7 Hz, 2H), 1.63-1.75 (m, 2H), 1.20-1.43 (m, 10H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.7, 147.6, 137.6, 133.0, 128.53, 128.50, 121.1, 41.1, 31.7, 29.2, 29.1, 28.6, 27.3, 22.6, 14.0. IR (neat): 2927.7, 2856.4, 1670.2, 1606.6, 1456.2, 1224.7 cm^{-1}. EI-MS: *m/z* 280 (0.2%, $[M+2]^+$), 279 (0.3, $[M+1]^+$), 278 (0.9, $[M]^+$), 243 (22, $[M-Cl]^+$), 105 (100), 77 (37). Anal. Calcd. for $C_{17}H_{23}ClO$: C, 73.23; H, 8.31. Found: C, 73.37; H, 8.24.

(*Z*)-1-Chloro-1,2-diphenylethene (**4a**)[19]



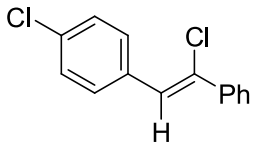
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.75 (m, 4H), 7.31-7.43 (m, 6H), 7.07 (s, 1H).

(*Z*)-1-Chloro-2-(4-methylphenyl)-1-phenylethene (**4b**)[6]



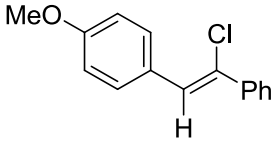
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62-7.71 (m, 4H), 7.31-7.43 (m, 3H), 7.21 (d, J = 8.2 Hz, 2H), 7.04 (s, 1H), 2.38 (s, 3H).

(*Z*)-1-Chloro-2-(4-chlorophenyl)-1-phenylethene (**4c**)[6]



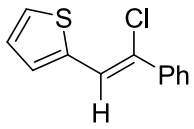
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.71 (m, 4H), 7.34-7.44 (m, 5H), 7.01 (s, 1H).

(*Z*)-1-Chloro-2-(4-methoxylphenyl)-1-phenylethene (**4d**)[20]



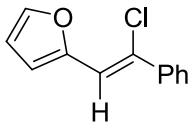
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 5/1) and identified by ^{1}H NMR spectrum according to the reported data. Pale yellow solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 7.3 Hz, 2H), 7.29-7.40 (m, 3H), 6.99 (s, 1H), 6.92 (d, J = 8.6 Hz, 2H), 3.82 (s, 3H).

(*Z*)-1-Chloro-2-(2-thienyl)-1-phenylethene (**4e**)



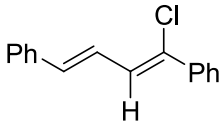
Isolated by column chromatography (silica gel, hexane). Colorless amorphous. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (m, 2H), 7.29-7.39 (m, 6H), 7.05-7.07 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 138.8, 138.2, 130.2, 129.5, 128.5, 128.4, 127.2, 126.4, 126.3, 119.8. IR (neat): 3062.7, 1488.9, 1444.6, 1211.2, 1193.9, 761.8, 690.5 cm^{-1}. EI-MS: *m/z* 222 (20%, $[M+2]^+$), 221 (12, $[M+1]^+$), 220 (65, $[M]^+$), 184 (100), 152 (39), 92 (45). ESI-HRMS: Calcd. for $C_{12}H_9ClSH$ ($[M+H]^+$), 221.0186. Found, 221.0186.

(*Z*)-1-Chloro-2-(2-furyl)-1-phenylethene (**4f**)



Isolated by column chromatography (silica gel, hexane). Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.69 (m, 2H), 7.43 (d, J = 1.8 Hz, 1H), 7.29-7.40 (m, 3H), 7.09 (d, J = 3.6 Hz, 1H), 7.07 (s, 1H), 6.49 (dd, J = 3.6, 1.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.0, 142.1, 138.1, 129.8, 128.7, 128.4, 126.2, 115.2, 111.9, 111.6. IR (neat): 1481.2, 1444.6, 1020.3, 956.6, 740.6, 690.5 cm^{-1}. EI-MS: *m/z* 206 (32%, $[M+2]^+$), 205 (18, $[M+1]^+$), 204 (100, $[M]^+$), 169 (97), 141 (90). ESI-HRMS: Calcd. for $C_{12}H_9ClOH$ ($[M+H]^+$), 205.0415. Found, 205.0415.

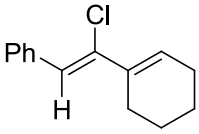
(*Z*,*E*)-1-Chloro-1,4-diphenyl-1,3-butadiene (**4g**)[6]



Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.7 Hz,

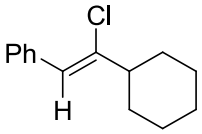
2H), 7.50 (d, J = 7.2 Hz, 2H), 7.24-7.42 (m, 7H), 6.94 (d, J = 10.4 Hz, 1H), 6.80 (d, J = 15.4 Hz, 1H).

(*Z*)-1-Chloro-1-(1-cyclohexenyl)-2-phenylethene (**4h**)[6]



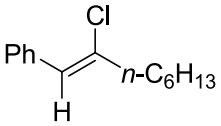
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 7.5 Hz, 2H), 7.32-7.40 (m, 2H), 7.24-7.30 (m, 1H), 6.70 (s, 1H), 6.50-6.64 (m, 1H), 2.34-2.42 (m, 2H), 2.22-2.27 (m, 2H), 1.72-1.78 (m, 2H), 1.60-1.70 (m, 2H).

(*Z*)-1-Chloro-1-(1-cyclohexyl)-2-phenylethene (**4i**)



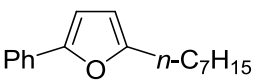
Isolated by column chromatography (silica gel, hexane). Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 7.2 Hz, 2H), 7.32 (t, J = 7.3 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 6.45 (s, 1H), 2.28-2.36 (m, 1H), 1.91-1.96 (m, 2H), 1.80-1.86 (m, 2H), 1.67-1.73 (m, 1H), 1.10-1.52 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.5, 135.4, 129.1, 128.0, 127.2, 122.2, 48.7, 31.6, 26.1, 25.9. IR (neat): 2929.7, 2852.5, 1446.5, 752.2, 694.3 cm^{-1}. EI-MS: m/z 222 (4%, $[M+2]^+$), 221 (3, $[M+1]^+$), 220 (14, $[M]^+$), 185 (41, $[M–Cl]^+$), 117 (59), 18 (100). Anal. Calcd. for $C_{14}H_{17}Cl$: C, 76.18; H, 7.76. Found: C, 76.31; H, 8.02.

(*Z*)-2-Chloro-1-phenyl-1-octene (**4j**)[6]



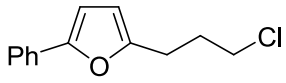
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.7 Hz, 2H), 7.34 (t, J = 7.2 Hz, 2H), 7.25 (t, J = 6.8 Hz, 1H), 6.46 (s, 1H), 2.48 (t, J = 7.2 Hz, 2H), 1.65 (quintet, J = 7.2 Hz, 2H), 1.28-1.40 (m, 6H), 0.90 (t, J = 6.8 Hz, 3H).

2-Heptyl-5-phenylfuran (**5a**)[21]



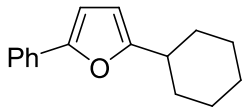
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.64 (m, 2H), 7.29-7.37 (m, 2H), 7.15-7.23 (m, 1H), 6.53 (d, J = 3.3 Hz, 1H), 6.04 (d, J = 3.3 Hz, 1H), 2.66 (t, J = 7.4 Hz, 2H), 1.68 (quintet, J = 7.4 Hz, 2H), 1.23-1.42 (m, 8H), 0.88 (t, J = 7.0 Hz, 3H).

2-(3-Chloropropyl)-5-phenylfuran (**5b**)



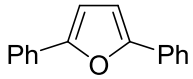
Isolated by column chromatography (silica gel, hexane). Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.64 (m, 2H), 7.32-7.38 (m, 2H), 7.19-7.24 (m, 2H), 6.53 (d, J = 3.2 Hz, 1H), 6.11 (d, J = 3.2 Hz, 1H), 3.59 (t, J = 6.3 Hz, 2H), 2.89 (t, J = 7.3 Hz, 2H), 2.15 (quintet, J = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.1, 152.6, 130.9, 128.6, 126.9, 123.3, 107.8, 105.6, 44.1, 30.9, 25.3 . IR (neat): 2958.6, 1595.0, 1548.7, 1487.0, 1444.6, 1024.1, 759.9, 692.4 cm^{-1}. EI-MS: *m/z* 222 (7%, $[M+2]^+$), 221 (3, $[M+1]^+$), 220 (24, $[M]^+$), 157 (100), 128 (22), 77 (18). ESI-HRMS: Calcd. for $C_{13}H_{14}ClO$ ($[M+H]^+$), 221.0728. Found, 221.0728.

2-Cyclohexyl-5-phenylfuran (**5c**)[22]



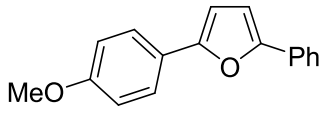
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 7.2 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 7.20 (t, J = 7.2 Hz, 2H), 6.54 (d, J = 4.4 Hz, 1H), 6.03 (dd, J = 3.2, 0.9 Hz, 1H), 2.62-2.71 (m, 1H), 2.03-2.13 (m, 2H), 1.70-1.87 (m, 3H), 1.20-1.49 (m, 5H).

2,5-Diphenylfuran (**5d**)[23]



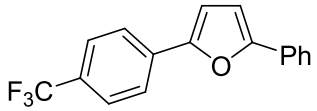
Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 7.2 Hz, 4H), 7.41 (t, J = 7.7 Hz, 4H), 7.22-7.27 (m, 2H), 6.74 (s, 2H).

2-(4-Methoxyphenyl)-5-phenylfuran (**5e**)[24]



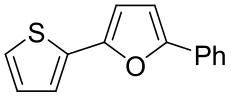
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 3/1) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, J = 8.6, 1.4 Hz, 2H), 7.66 (d, J = 9.0 Hz, 2H), 7.35-7.41 (m, 2H), 7.21-7.26 (m, 2H), 6.92 (d, J = 9.0 Hz, 2H), 6.69 (d, J = 3.6 Hz, 1H), 6.57 (d, J = 3.6 Hz, 1H), 3.81 (s, 3H).

2-Phenyl-5-(4-trifluoromethylphenyl)furan (**5f**)[25]



Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. White solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 6.8 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.28-7.33 (m, 1H), 6.86 (d, J = 3.2 Hz, 1H), 6.77 (d, J = 3.2 Hz, 1H).

2-Phenyl-5-(2-thienyl)furan (**5g**)[23]

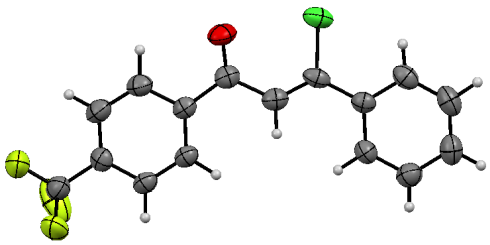


Isolated by column chromatography (silica gel, hexane) and identified by ^{1}H NMR spectrum according to the reported data. Colorless solids: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, J = 8.6, 1.4 Hz, 2H), 7.38 (t, J = 7.7 Hz, 2H), 7.31 (dd, J = 3.6, 1.4 Hz, 1H), 7.21-7.28 (m, 2H), 7.04 (dd, J = 5.0, 3.6 Hz, 1H), 6.68 (d, J = 3.6 Hz, 1H), 6.56 (d, J = 3.6 Hz, 1H).

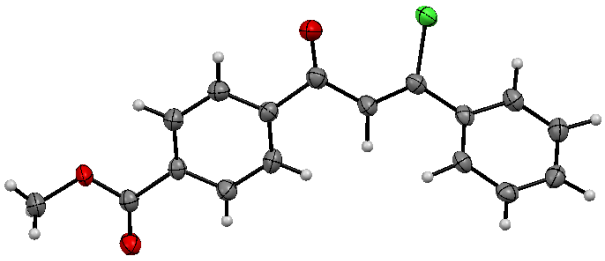
$IrCl_2(CO)(Ph)(RuPhos)$ (**6)**

Off-white solids: m.p. 168-170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (t, J = 9.1 Hz, 1H), 7.50-7.52 (m, 2H), 7.46 (t, J = 8.2 Hz, 2H), 7.38 (t, J = 7.7 Hz, 1H), 7.24-7.30 (m, 1H), 6.85-6.92 (m, 5H), 5.51 (septet, J = 6.3 Hz, 1H), 4.61 (septet, J = 6.3 Hz, 1H), 2.00-2.34 (m, 3H), 1.27-1.98 (m, 19H), 1.20 (d, J = 5.6 Hz, 3H), 1.01-1.18 (m, 6H) 0.61 (d, J = 6.3 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.2 (d, $J_{C\text{-}P}$ = 6.7 Hz), 156.2, 154.6, 139.4, 138.8 (d, $J_{C\text{-}P}$ = 6.7 Hz), 135.1 (d, $J_{C\text{-}P}$ = 9.5 Hz), 133.7 (d, $J_{C\text{-}P}$ = 4.8 Hz), 131.1, 130.0, 129.2 (d, $J_{C\text{-}P}$ = 2.9 Hz), 127.9 (d, $J_{C\text{-}P}$ = 50.3 Hz) 127.0, 126.7, (d, $J_{C\text{-}P}$ = 9.5 Hz), 124.3, 123.6 (br), 115.7, 112.4 (d, $J_{C\text{-}P}$ = 4.8 Hz), 110.4, 80.5, 71.0, 40.8 (d, $J_{C\text{-}P}$ = 31.5 Hz), 36.3 (d, $J_{C\text{-}P}$ = 27.7 Hz), 30.7 (d, $J_{C\text{-}P}$ = 2.9 Hz), 30.5 (d, $J_{C\text{-}P}$ = 5.7 Hz), 29.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 28.0, 27.9, 27.9, 27.5 (d, $J_{C\text{-}P}$ = 2.9 Hz), 27.4 (d, $J_{C\text{-}P}$ = 4.8 Hz), 26.9 (d, $J_{C\text{-}P}$ = 12.4 Hz), 25.8 (d, $J_{C\text{-}P}$ = 4.8 Hz), 22.9, 22.6, 22.5, 21.1. ^{31}P{^{1}H} NMR (160 MHz, $CDCl_3$): δ 5.96. IR (KBr): 2927.7, 2036.7, 1452.3, 1110.9, 1029.9 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 771 ([M–Cl–CO]$^+$), 736 ([M–2Cl–CO]$^+$), 687 ([M–2Cl–Ph]$^+$). Anal. Calcd. for $C_{37}H_{48}Cl_2IrO_3P{\cdot}0.5CH_2Cl_2$: C, 51.34; H, 5.63. Found: C, 51.24; H, 5.61.

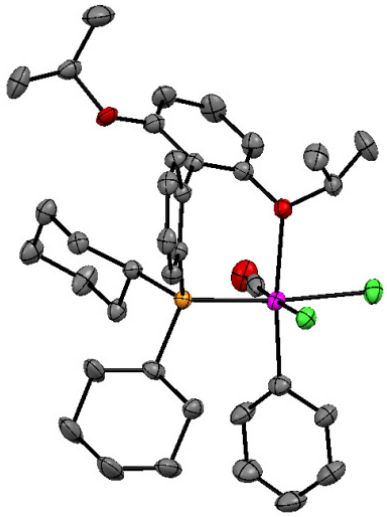
X-ray Diffraction Studies of 3e, 3f and 6



Single crystal of **3e** was obtained by recrystallization from hot hexane solution. Crystal data for **3e**: $C_{16}H_{10}ClF_3O$, M = 310.70, monoclinic, space group = $P2_1/c$ (#14), a = 13.077(11) Å, b = 7.098(6) Å, c = 14.856(12) Å, β = 101.902(14)°, V = 1349(2) Å^3, Z = 4, density (calc.) = 1.529, total reflections collected = 9615, unique reflections = 3079 (R_{int} = 0.065), GOF = 1.005. The final $R1$ factor was 0.0597 ($I>2\sigma(I)$) ($wR2$ = 0.0748, all data).



Single crystal of **3f** was obtained by recrystallization from hot hexane solution. Crystal data for **3f**: $C_{17}H_{13}ClO_3$, M = 300.74, monoclinic, space group = $P2_1/a$ (#14), a = 14.7624(15) Å, b = 5.7017(6) Å, c = 16.5862(15) Å, β = 94.381(6)°, V = 1392.0(2) Å^3, Z = 4, density (calc.) = 1.435, total reflections collected = 9680, unique reflections = 3136 (R_{int} = 0.047), GOF = 0.962. The final $R1$ factor was 0.0437 ($I>2\sigma(I)$) ($wR2$ = 0.0584, all data).



Single crystal of **6** was obtained by slow evaporation from CH_2Cl_2/hexane solution. Crystal data for **6**: $C_{75}H_{98}Cl_6Ir_2O_6P_2$, M = 1754.70, monoclinic, space group = $P2_1/a$ (#14), a = 19.5083(10) Å, b = 18.2986(5) Å, c = 22.2170(10) Å, β = 113.4000(19)°, V = 7278.6(5) Å^3, Z = 4, density (calc.) = 1.601, total reflections collected = 53366, unique reflections = 16618 (R_{int} = 0.057), GOF = 1.004. The final $R1$ factor was 0.0373 ($I>2\sigma(I)$) ($wR2$ = 0.0907, all data).

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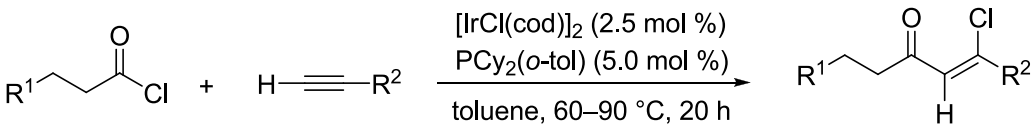
Chapter 3

Iridium-Catalyzed Addition of Aliphatic Acid Chlorides to Terminal Alkynes without Decarbonylation

Aliphatic acid chlorides are successfully added to terminal alkynes to afford (*Z*)-*β*-chloroalkenyl ketones regio- and stereoselectively in the presence of the iridium catalyst. The present catalytic reaction could proceed smoothly without undesired decarbonylation and *β*-hydride elimination in the absence of atmosphere of carbon monoxide and directing groups on substrates. A wide range of aliphatic acid chlorides and terminal alkynes could be applied to the reaction affording the corresponding adducts in high yields.



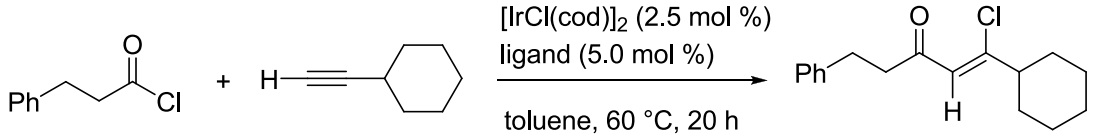
3-1. Introduction

In the Chapter 2, the author has disclosed that the iridium-catalyzed addition of acid chlorides to terminal alkynes to afford *β*-chloro-α,*β*-unsaturated ketones regio- and stereoselectively. However, the primitive catalyst was limited to only aromatic acid chlorides and aliphatic acid chlorides could not apply to the addition reaction due to facile decarbonylation followed by *β*-hydride elimination. Generally, to suppress undesired decarbonylation and *β*-hydride elimination, it would be required an atmosphere of carbon monoxide[1] and directing groups[2] to stabilize acyl-species. These strategies must be reliable albeit the practicality and substrate scope are considerably limited. Therefore, it is highly desirable to establish the catalytic system in the absence of external CO pressure and directing groups. In the Chapter 3, the author describes that an iridium complex successfully catalyzes the regio- and stereoselective addition of common *aliphatic* acid chlorides to terminal alkynes without decarbonylation.

3-2. Results and Discussion

First, the reaction of hydrocinnamoyl chloride (**1a**) and cyclohexylacetylene (**2a**) was carried out employing various ligands with a catalytic amount of $[IrCl(cod)]_2$ in toluene at 60 °C for 20 h (Table 3-1). When NHC ligands[3] such as IPr and IMes were used under the conditions for aromatic acid chlorides in Chapter 2,[4] an addition product (**3aa**) was obtained in very low yields (entries 1 and 2). By the use of PCy_3 and PCy_2Ph, the addition reaction slightly proceeded affording **3aa** in 23% and 28% yields, respectively (entry 4 and 5). In the cases of PCy_2(*o*-biphenyl), MePhos[5] and XPhos[5], the yields of **3aa** improved moderately (entries 6–8). When RuPhos[5], which worked in decarbonylative addition of aromatic acid chlorides to terminal alkynes in Chapter 2,[4] was used, no adduct was obtained at all (entry 9). PCy_2(*o*-tol) was most effective as a ligand to provide **3aa** in 93% yield regio- and stereoselectively (entry 10). Significantly, this reaction was unnecessary to use external CO and directing groups on substrates to prevent decarbonylation as well as *β*-hydride elimination. As for solvents, other solvents such as dioxane and 1,2-dichloroethane also work well to afford **3aa** in 84% and 72% yields, respectively.

Table 3-1. Effect of ligands on the iridium-catalyzed addition of hydrocinnamoyl chloride (**1a**) to cyclohexylacetylene (**2a**).[a]



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

Entry	ligand	**3aa** % yield[b]
1	IPr	8
2	IMes	3
3	PPh_3	0
4	PCy_3	23
5	PCy_2Ph	28
6	PCy_2(*o*-biphenyl)	60
7	MePhos	69
8	XPhos	67
9	RuPhos	0
10	PCy_2(*o*-tol)	93 (87)[c]

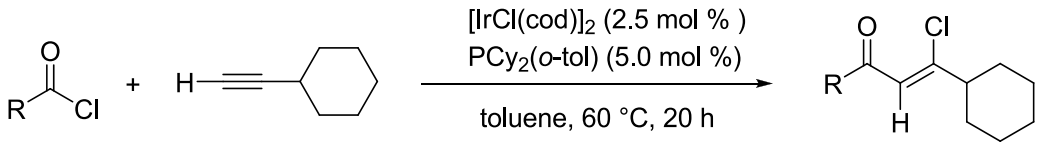
[a] Conditions: **1a** (0.50 mmol), **2a** (0.75 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), ligand (0.025 mmol, 5.0 mol %), solvent (1.0 mL), 60 °C, 20 h. [b] Determined by GC analysis. [c] Isolated yield.

In the presence of the iridium catalyst, various aliphatic acid chlorides **1** reacted with **2a**, affording the corresponding *β*-chloro-α,*β*-unsaturated ketones (**3**) regio- and stereoselectively, as shown in Table 3-2. Propanoyl- (**1b**), octanoly- (**1c**) and 3,5,5-trimethylhexanoyl- (**1d**) chloride having *β*-hydrogen on the sp^3 carbon provided **3ba**–**da** in high yields without decarbonylation (entries 1–3). Secondary alkyl acid chlorides **1e**–**g** smoothly reacted with **2a** at 90 °C to afford **3ea**–**ga** in high yields (entries 4–6). The regio- and stereochemistry of all products was unambiguously determined by the aid of 2D-NMR spectroscopy. The *Z*-configuration of **3ga** was further confirmed by a single-crystal X-ray diffraction study. Unfortunately, tertiary alkyl acid chlorides such as pivaloyl chloride and 1-adamantanecarbonyl chloride did not participate in the reaction, possibly due to the steric hindrance. Phenylacetyl chloride derivatives with electron-rich (**1i** and **1j**) and electron-poor (**1k**–**m**) phenyl moieties participated in the addition to afford **3ha**–**ma** in good to high yields (entries 7–12). 1-Naphthyl- and 3-thienylacetyl chlorides afforded the corresponding adducts **3na** and **3oa** in good yields, respectively (entries 13 and 14). Functional groups such as

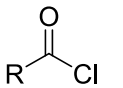
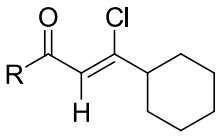
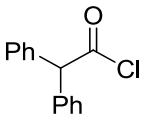
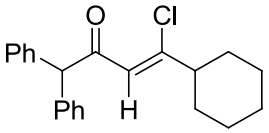
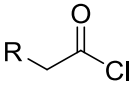
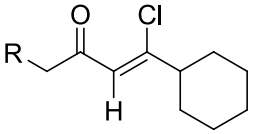
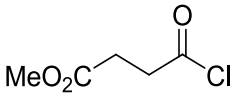
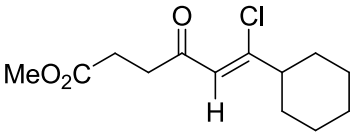
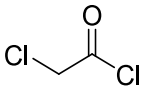
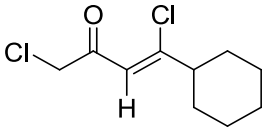
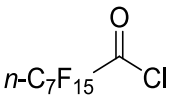
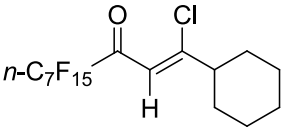
phenyl ether and ester can be well tolerated in the reaction (entries 15 and 16). Moreover, *β*-chloroacetyl chloride (**1r**) and perfluorinated acid chloride (**1s**), which were reported in previous rhodium-catalyzed system,[6] can be applied to the iridium-catalyzed system. In the case of **1s**, IrCl(cod)(IPr) was effective as a catalyst precursor to give **3sa** in 68% yield.

Next, the scope of terminal alkynes **2** was examined with **1a** as an acid chloride substrate (Table 3-3). Various aliphatic and aromatic terminal alkynes afforded the corresponding *β*-chloro-α,*β*-unsaturated ketones regio- and stereoselectively. 1-Octyne (**2b**) and *t*-butylacetylene (**2c**) smoothly provided **3ab** and **3ac** in high yields without decarbonylation as well as *β*-hydride elimination (entries 1 and 2). Functional groups such as chloro, ester and phthalimide could be tolerated in the reaction and these substrates gave high yields of adducts **3ad**–**ag** (entries 3–6). The reaction of enyne **2h** was successful to give **3ah** in 80% yield (entry 7). Phenylacetylene derivatives (**2i**–**n**) with electron-donating or electron-withdrawing groups also worked well in the reaction at 90 °C (entries 8–13). Internal alkynes, however, did not afforded desired products at all.

Table 3-2. Iridium-catalyzed addition of acid chlorides (**1**) to **2a**.[a]

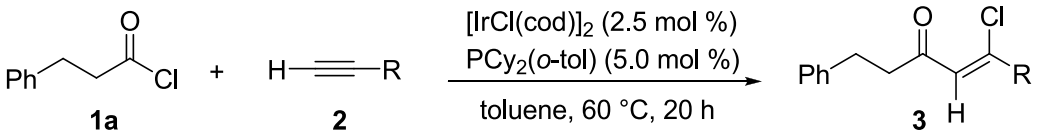


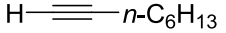
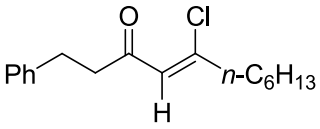
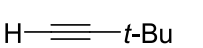
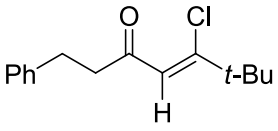
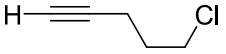
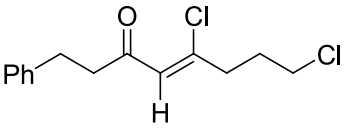
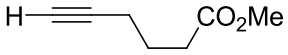
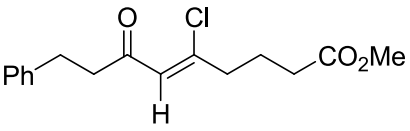
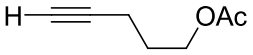
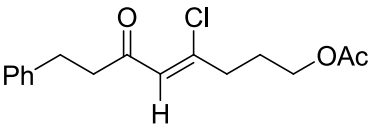
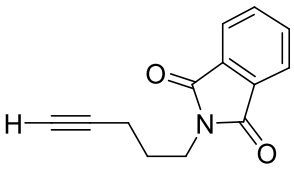
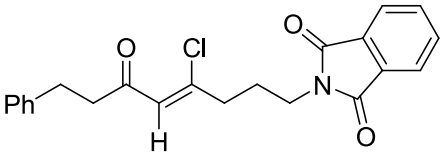
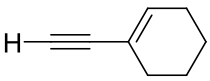
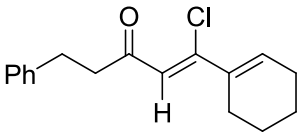
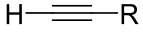
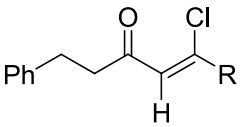
1 **2a** **3**

entry	**1**		**3**		% yield[b]
1		R = Et **1b**		**3ba**	82
2		R = *n*-C_7H_{15} **1c**		**3ca**	91
3[c]		R = 3,5,5-$Me_3C_5H_8$ **1d**		**3da**	83
4[c]		R = *c*-C_3H_5 **1e**		**3ea**	99
5[c]		R = *c*-C_6H_{11} **1f**		**3fa**	92
6[c]		**1g**		**3ga**	79
7		R = Ph **1h**		**3ha**	89
8[c]		R = 4-MeC_6H_4 **1i**		**3ia**	74
9		R = 4-$MeOC_6H_4$ **1j**		**3ja**	64
10		R = 4-ClC_6H_4 **1k**		**3ka**	76
11		R = 4-BrC_6H_4 **1l**		**3la**	88
12		R = 4-$NO_2C_6H_4$ **1m**		**3ma**	51
13[c]		R = 1-naphthyl **1n**		**3na**	76
14		R = 3-thienyl **1o**		**3oa**	77
15		R = PhO **1p**		**3pa**	82
16		**1q**		**3qa**	85
17		**1r**		**3ra**	98
18[c,d]		**1s**		**3sa**	68

[a] Conditions: acid chlorides (0.50 mmol), **2a** (0.75 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), PCy_2(*o*-tol) (0.025 mmol, 5.0 mol %), toluene (1.0 mL), 60 °C, 20 h. [b] Isolated yields. [c] 90 °C. [d] Using IrCl(cod)(IPr) (0.025 mmol, 5.0 mol %) as a catalyst.

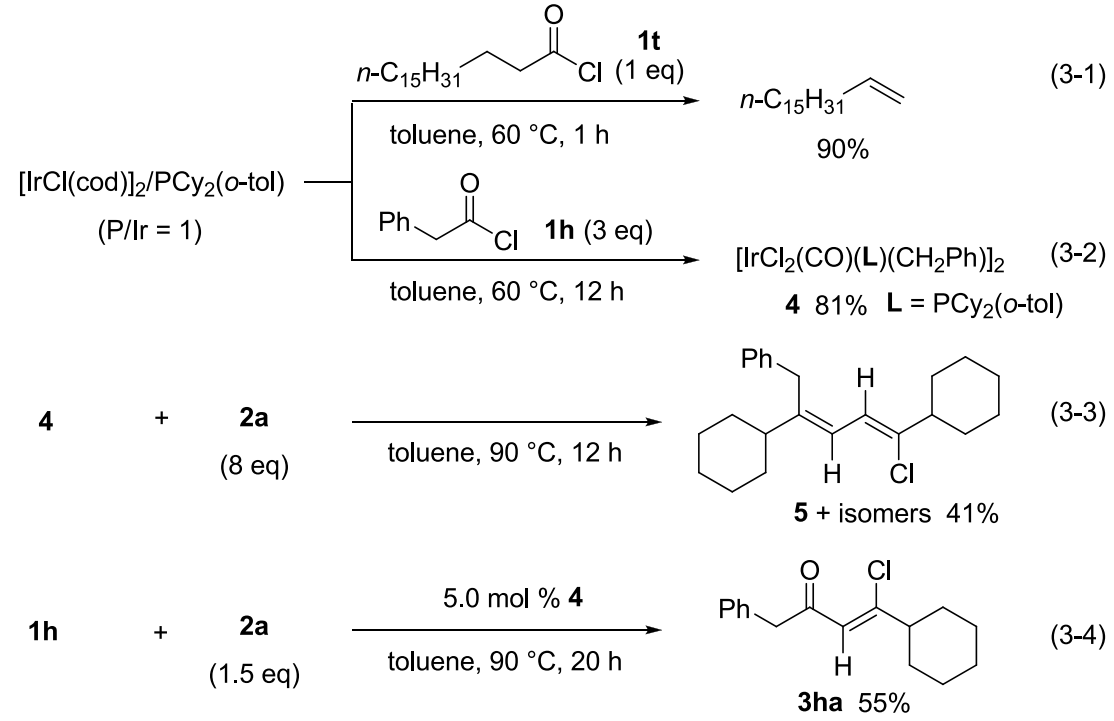
Table 3-3. Iridium-catalyzed addition of **1a** to terminal alkynes (**2**).[a]



entry	2		3		% yield[b]
1		**2b**		**3ab**	86
2		**2c**		**3ac**	89
3		**2d**		**3ad**	77
4		**2e**		**3ae**	76
5		**2f**		**3af**	79
6		**2g**		**3ag**	84
7		**2h**		**3ah**	80
8[c]		R = Ph **2i**		**3ai**	81
9[c]		R = 4-MeC_6H_4 **2j**		**3aj**	88
10[c]		R = 4-$MeOC_6H_4$ **2k**		**3ak**	81
11[c]		R = 4-ClC_6H_4 **2l**		**3al**	75
12[c]		R = 4-BrC_6H_4 **2m**		**3am**	58
13[c]		R = 4-PhC_6H_4 **2n**		**3an**	78

[a] Conditions: **1a** (0.50 mmol), alkyne (0.75 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), PCy_2(*o*-tol) (0.025 mmol, 5.0 mol %), toluene (1.0 mL), 60 °C, 20 h. [b] Isolated yields. [c] 90 °C.

To gain further insight into the mechanism, the reaction of $[IrCl(cod)]_2/PCy_2(o\text{-tol})$ (P/Ir =1) with acid chlorides was carried out. When stearoyl chloride (**1t**) was used, **1t** was converted completely at 60 °C for 1 h (eq 3-1). As a result, decarbonylation followed by β-hydride elimination occurred to give 1-heptadecene in 90% yield. On the other hand, **1h** reacted with $[IrCl(cod)]_2/PCy_2(o\text{-tol})$ at 60 °C for 12 h and a chloro-bridged binuclear iridium complex **4** was isolated in 81% yield (eq 3-2). The structure of **4** was confirmed by X-ray diffraction study (Figure 3-1).[7] These results are quite different from the reaction of IrCl(cod)(IPr) with aromatic acid chlorides, as described in Chapter 2.[4] Treatment of **4** with **2a** at 90 °C afforded diene **5** in 41% yield, as containing some unidentified isomers (eq 3-3). It was noteworthy that **4** catalyzed the addition of **1h** to **2a** providing the adduct **3ha** in 55% yield (eq 3-4).



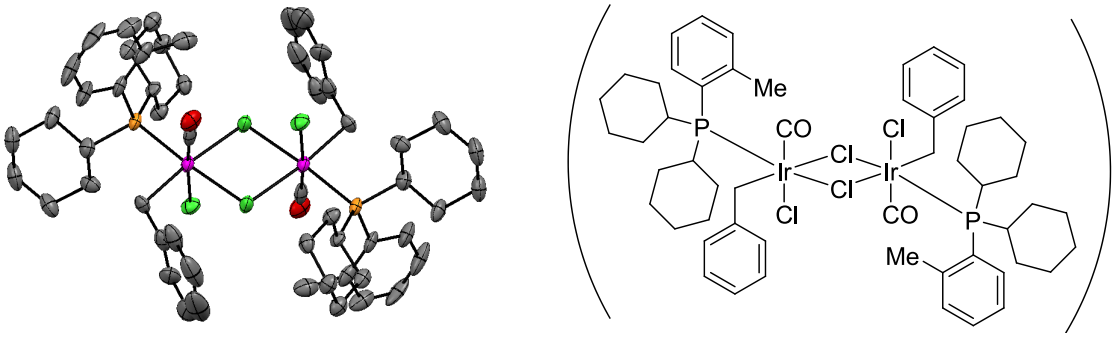
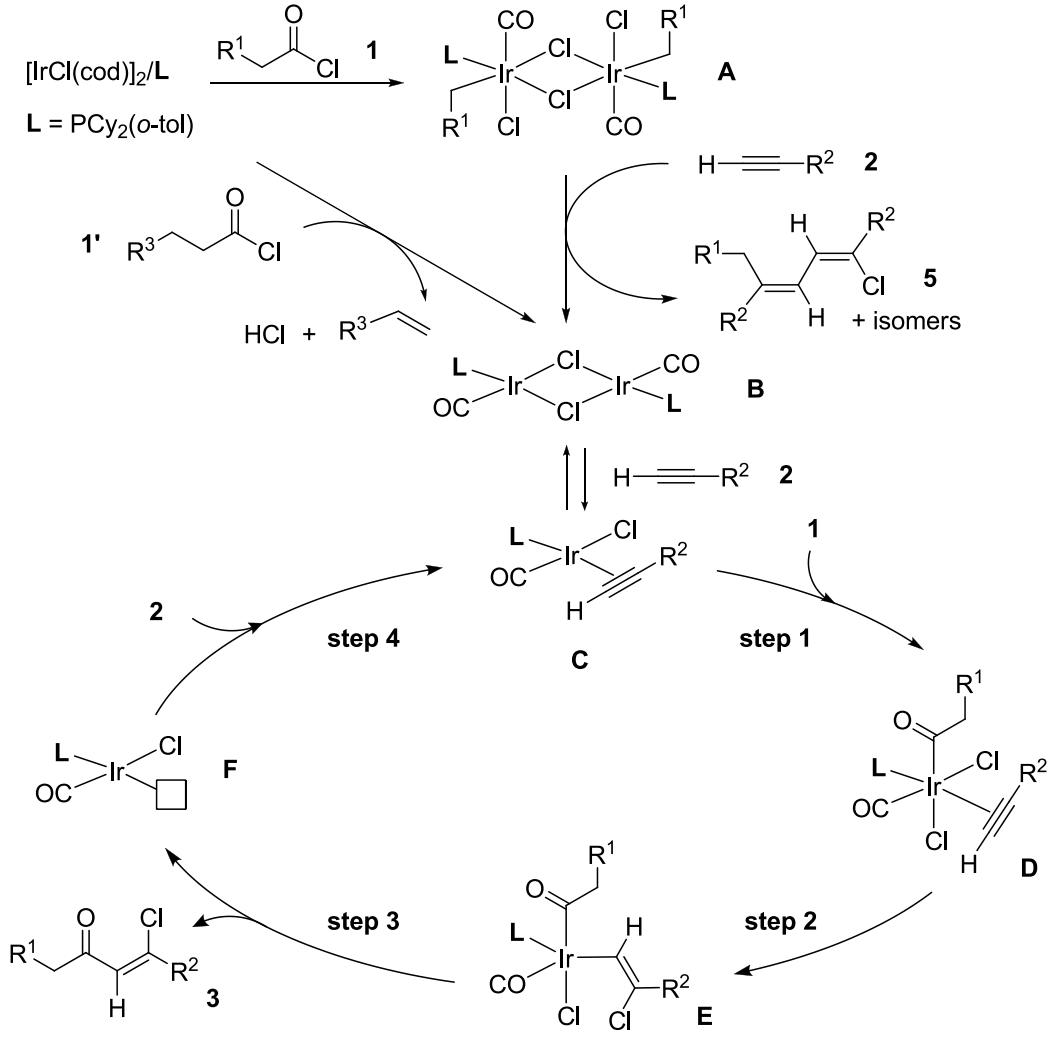


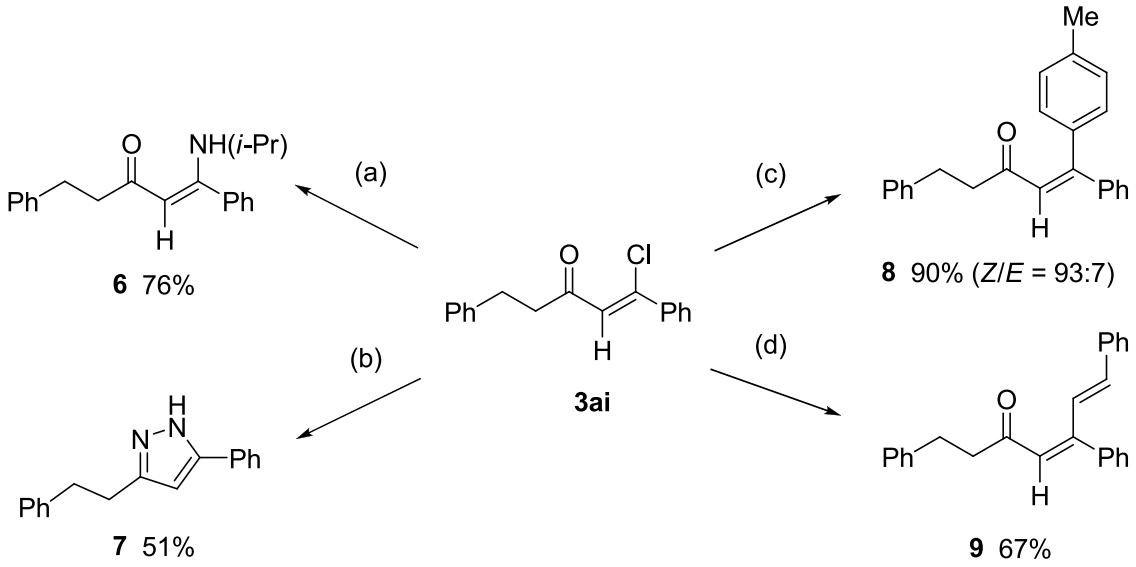
Figure 3-1. Single crystal structure of **4**.

A plausible reaction mechanism is shown in Scheme 3-1. In the case of **1** having no β-hydrogen on the sp^3 carbon, the oxidative addition of **1** to the iridium(I) species followed by decarbonylation affords binuclear iridium complex **A** confirmed by X-ray diffraction study. Subsequent insertion of two equivalent of terminal alkyne **2** would occur to provide dienes **5** and a binuclear iridium-carbonyl complex **B**. On the other hand, when **1'** having β-hydrogen on the sp^3 carbon is used, the iridium complex **B** might be generated directly with eliminations of alkene and HCl via decarbonylation followed by β-hydride elimination steps. The binuclear comoplex **B** would be dissociated to a mononuclear iridium species **C** by the aid of **2**. Oxidative addition of **1** toward **C** would provide an acyl-iridium intermediate **D** (step 1). Subsequent insertion of **2** into the iridium-chloro bond (step 2)[6,8] followed by reductive elimination from **E** could afford **3** as the product (step 3). The iridium complex **C** may regenerate via the coordination of **2** toward **F** (step 4).



Scheme 3-1. Plausible reaction mechanism.

The products for the addition of acid chlorides to alkynes, *β*-chloroalkenyl ketones **3**, are versatile intermediates in organic synthesis, especially for synthesis of heterocyclic compounds.[9] The synthetic utility of the adduct **3ai** was demonstrated in Scheme 3-2. The reaction with isopropylamine gave an (*Z*)-*β*-aminoalkenyl ketone **6** as a sole product via nucleophilic conjugated addition. The cyclization with hydrazine afforded a pyrazole **7**. The chloro functionality on **3ai** could transform in the palladium-catalyzed cross-coupling reactions such as Suzuki-Miyaura coupling. The reaction of **3ai** with *p*-tolylboronic acid proceeded to give **8** in 90% yield, as containing a small amount of stereoisomers determined by ^{1}H NMR measurement (*Z*/*E* = 93:7). The coupling reaction with *trans*-styrylboronic acid gave diene **9** in 67% yield as a single isomer.



Conditions: (a) *i*-PrNH$_2$ (20 eq), Et$_2$O, rt., 16 h. (b) $N_2H_4 \cdot H_2O$ (3 eq), EtOH, reflux, 5 h. (c) *p*-Tolylboronic acid (1.5 eq), Pd(OAc)$_2$ (2.0 mol %), SPhos (5.0 mol %), K_3PO_4 (2.0 eq), toluene, reflux, 18 h. (d) *trans*-Styrylboronic acid (1.5 eq), Pd(OAc)$_2$ (2.0 mol %), SPhos (5.0 mol %), K_3PO_4 (2.0 eq), toluene, reflux, 18 h.

Scheme 3-2. Transformation of *β*-chloroalkenyl ketone **3ai**.

3-3. Conclusion

Aliphatic acid chlorides were successfully added to terminal alkynes to afford (*Z*)-*β*-chloroalkenyl ketones regio- and stereoselectively in the presence of the iridium catalyst. The present catalytic reaction could proceed smoothly without undesired decarbonylation and *β*-hydride elimination in the absence of atmosphere of carbon monoxide and directing groups on substrates. In the reaction of the present iridium catalyst with phenylacetyl chloride, the binuclear carbonyl-iridium complex **4** was

isolated and **4** was the efficient catalyst for the addition of aliphatic acid chlorides to terminal alkynes.

3-4. Experimental Section

Instrumentation and Chemicals

All manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. All solvents were dried and purified by usual procedures.[10] Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. $[IrCl(cod)]_2$ was prepared according to the literature.[11] PCy_2(*o*-tol), PCy_2(*o*-biphenyl), MePhos, XPhos and RuPhos were purchased from Aldrich. Acid chlorides **1a**, **1b**, **1e**, **1j**, **1k** and **1s** were purchased from Aldrich. Acid chlorides **1c**, **1d**, **1f**, **1g**, **1h**, **1p**, **1r** and **1t** were purchased from TCI. Acid chloride **1q** was purchased from Wako. Acid chlorides **1i**,[12] **1l**,[13] **1m**,[14] **1n**[15] and **1o**[16] were prepared according to the literatures. Alkynes **2a**, **2c**, **2g**, **2h**, **2l** and **2m** were purchased from Aldrich. Alkynes **2b**, **2d** and **2i** were purchased from TCI. Alkynes **2e**, **2f**, **2j**, **2k** and **2n** were purchased from Wako. IR spectra were obtained on a SHIMADZU FTIR-8300 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^{1}H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). EI-MS were recorded on a Shimadzu GCMS-QP5050A with a direct inlet. High-resolution mass spectra (ESI-HRMS) were obtained with a JEOL SX-102A spectrometer. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using a Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). Melting points were measured on a Yanako MP-J3 apparatus. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$.

General procedure in Table 3-1

$IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and the ligand (0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1a** (74 μL, 0.50 mmol) and **2a** (98 μL, 0.75 mmol) were added to the flask and the mixture was heated at 60 °C

for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and added tetradecane (50 μL, 0.192 mmol) as an internal standard. The yield of **3aa** was determined by GC analysis.

General procedures for the iridium-catalyzed addition of acid chlorides (1) to terminal alkynes (2) (Tables 3-2 and 3-3)

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and PCy_2(*o*-tol) (7.2 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. An acid chloride (**1**) (0.50 mmol) and an alkyne (**2**) (0.75 mmol) were added to the flask and the mixture was stirred at 60 °C for 20 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product was isolated by silica gel column chromatography.

Procedure in eq 3-1

$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and PCy_2(*o*-tol) (14.4 mg, 0.050 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. Stearoyl chloride (**1t**) (0.050 mmol) and tetradecane (0.050 mmol) as an internal standard were added to the flask and the mixture was stirred at 60 °C for 1 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (2.0 ml) and the yield of 1-heptadecene was determined by GC analysis.

Procedure in eq 3-2

$[IrCl(cod)]_2$ (33.6 mg, 0.050 mmol) and PCy_2(*o*-tol) (28.8 mg, 0.10 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. Phenylacetyl chloride (**1h**) (0.30 mmol) was added to the flask and the mixture was stirred at 60 °C for 12 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the crude product was washed with diethyl ether (1 mL x 3) to give off-white solids of $[IrCl_2(CO)\{PCy_2(o\text{-tol})\}(CH_2Ph)]_2$ (**4**) (54.6 mg, 81% yield).

Procedure in eq 3-3

The iridium complex **4** (33.5 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) and **2a** (26 μL, 0.20 mmol) were added to the flask and the mixture was heated at 90 °C for 12 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product was isolated by silica gel column chromatography and GPC to give **5**, as containing some unidentified isomers (7.0 mg, 41% yield).

Procedure in eq 3-4

The iridium complex **4** (8.4 mg, 0.00626 mmol) was added to a 10 mL Schlenk flask with a reflux condenser. The flask was evacuated and backfilled with argon three times. Then degassed toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1h** (33 μL, 0.25 mmol) and **2a** (49 μL, 0.375 mmol) were added to the flask and the mixture was heated at 90 °C for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (2.0 mL) and added tetradecane (25 μL, 0.096 mmol) as an internal standard. The yield of the product **3ha** was determined by GC analysis.

Transformation of *β*-chloroalkenyl ketone (3ai) in Scheme 3-2

Synthesis of **6**: **3ai** (81.2 mg, 0.30 mmol) was added to a 10 mL Schlenk flask with a magnetic stir bar. Then EtOH (1.0 mL) and NH_2(*i*-Pr) (515 μL, 6.0 mmol, 20 eq) were added to the flask and the resultant solution was stirred at room temperature for 16 h. The mixture was evaporated and the product **6** was isolated in 76% yield by silica gel column chromatography using hexane–EtOAc (20:1 then 10:1) as an eluent.

Synthesis of **7**: **3ai** (81.2 mg, 0.30 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. Then EtOH (1.0 mL) and $N_2H_4 \cdot H_2O$ (44 μL, 0.90 mmol, 3 eq) were added to the flask and the resultant solution was stirred under reflux (bath temp. 95 °C) for 5 h. The mixture was evaporated and the product **7** was isolated in 51% yield by silica gel column chromatography using hexane–EtOAc (3:1 then 1:1) as an eluent.

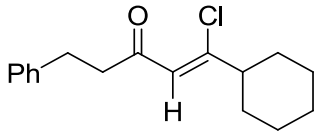
Synthesis of **8**: **3ai** (81.2 mg, 0.30 mmol), $Pd(OAc)_2$ (1.3 mg, 0.0060 mmol, 2.0 mol %) and SPhos (6.2 mg, 0.015 mmol, 5.0 mol %) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and

backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. *p*-Tolylboronic acid (61.2 mg, 0.45 mmol, 1.5 eq) and K_3PO_4 (127 mg, 0.60 mmol) were added to the flask and the mixture was stirred under reflux (bath temp. 120 °C) for 18 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product **8** was isolated in 90% yield (*Z*/*E* = 93:7, determined by ^{1}H NMR) by silica gel column chromatography using hexane–EtOAc (25:1) as an eluent.

Synthesis of **9**: **3ai** (81.2 mg, 0.30 mmol), $Pd(OAc)_2$ (1.3 mg, 0.0060 mmol, 2.0 mol %) and SPhos (6.2 mg, 0.015 mmol, 5.0 mol %) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. *trans*-Styrylboronic acid (66.6 mg, 0.45 mmol, 1.5 eq) and K_3PO_4 (127 mg, 0.60 mmol) were added to the flask and the mixture was stirred under reflux (bath temp. 120 °C) for 18 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product **9** was isolated in 67% yield by silica gel column chromatography using hexane–EtOAc (20:1) as an eluent.

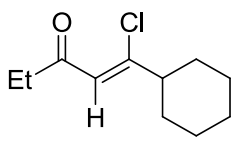
Characterization of the Compounds

(*Z*)-1-Chloro-1-cyclohexyl-5-phenyl-1-penten-3-one (**3aa**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 120 mg, 87% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.24 (m, 2H), 7.20-7.15 (m, 3H), 6.21 (s, 1H), 2.93 (m, 4H), 2.24 (tt, J = 11.3, 3.2 Hz, 1H), 1.88-1.79 (m, 4H), 1.71-1.68 (m, 1H), 1.40-1.11 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.1, 151.9, 141.0, 128.35, 128.30, 125.9, 122.2, 48.9, 45.6, 31.2, 29.8, 25.8, 25.6. IR (neat): 2929.7, 2854.5, 1697.2, 1604.7, 1496.7, 698.2 cm^{-1}. EI-MS: *m/z* 278 (0.1%, $[M+2]^+$), 276 (0.5, $[M]^+$), 241 (100), 171 (27), 91 (75). ESI-HRMS: Calcd. for $C_{17}H_{21}ClONa$ ($[M+Na]^+$), 229.1173. Found, 299.1172.

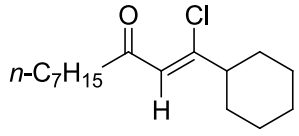
(*Z*)-1-Chloro-1-cyclohexyl-1-penten-3-one (**3ba**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 30/1). Pale yellow oil, 82.3 mg, 82% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 (s, 1H), 2.69 (q, J = 7.2 Hz, 2H), 2.27 (tt, J = 11.3, 3.2 Hz, 1H), 1.95-1.80 (m, 4H), 1.73-1.66 (m, 1H), 1.44-1.13 (m, 5H), 1.10 (t, J = 7.7

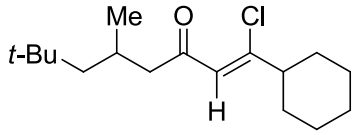
Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.7, 151.3, 122.0, 48.9, 37.2, 31.2, 25.8, 25.6, 7.7. IR (neat): 2931.6, 2854.4, 1701.1, 1608.5, 1450.4 cm^{-1}. EI-MS: *m/z* 202 (2%, $[M+2]^+$), 200 (7, $[M]^+$), 173 (47), 171 (100), 135 (42). ESI-HRMS: Calcd. for $C_{11}H_{17}ClONa$ ($[M+Na]^+$), 223.0860. Found, 223.0861.

(*Z*)-1-Chloro-1-cyclohexyl-1-decen-3-one (**3ca**)



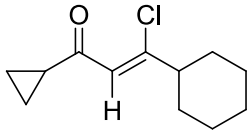
Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 123 mg, 91% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 6.24 (s, 1H), 2.58 (t, J = 7.2 Hz, 2H), 2.26 (tt, J = 10.9, 3.2 Hz, 1H), 1.91-1.81 (m, 4H), 1.72-1.69 (m, 1H), 1.63-1.57 (m, 2H), 1.43-1.15 (m, 13H), 0.87 (t, J = 6.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.5, 151.2, 122.2, 48.9, 44.1, 31.6, 31.2, 29.07, 29.01, 25.8, 25.6, 23.8, 22.5, 14.0. IR (neat): 2929.7, 2854.5, 1701.1, 1608.5, 1456.2 cm^{-1}. EI-MS: *m/z* 272 (0.1%, $[M+2]^+$), 270 (0.3, $[M]^+$), 235 (6), 186 (100), 171 (55). Anal. Calcd. for $C_{16}H_{27}ClO$: C, 70.95; H, 10.05. Found: C, 70.98; H, 10.11.

(*Z*)-1-Chloro-1-cyclohexyl-5,7,7-trimethyl-1-octen-3-one (**3da**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 30/1). Pale yellow oil, 118 mg, 83% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 6.22 (s, 1H), 2.58-2.51 (m, 1H), 2.47-2.40 (m, 1H), 2.30-2.25 (m, 1H), 2.17-2.06 (m, 1H), 1.93-1.77 (m, 4H), 1.75-1.66 (m, 1H), 1.43-1.06 (m, 7H), 0.96 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.0, 151.1, 122.3, 53.8, 50.7, 48.9, 31.2, 31.0, 29.9, 26.0, 25.8, 25.7, 22.8. IR (neat): 2933.5, 2856.4, 1693.4, 1593.1, 1450.4, 1365.5 cm^{-1}. EI-MS: *m/z* 286 (0.1%, $[M+2]^+$), 284 (0.2, $[M]^+$), 269 (2), 213 (9), 188 (20), 186 (68), 171 (31), 57 (100) ESI-HRMS: Calcd. for $C_{17}H_{29}ClONa$ ($[M+Na]^+$), 307.1799. Found, 307.1801.

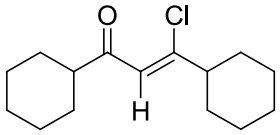
(*Z*)-3-Chloro-3-cyclohexyl-1-cyclopropyl-2-propen-1-one (**3ea**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 30/1). Pale yellow oil, 105 mg, 99% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 6.35 (s, 1H), 2.28 (tt, J = 10.9, 2.7 Hz, 1H), 2.21-2.15 (m, 1H), 1.94-1.78 (m, 4H), 1.75-1.65 (m, 1H), 1.44-1.07 (m, 7H), 0.97-0.93 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.4, 150.8, 122.4, 48.7, 31.2, 25.8, 25.6, 22.1, 11.7. IR (neat): 2931.6, 2854.5, 1683.7, 1604.7, 1450.4, 1384.8, 1080.1 cm^{-1}.

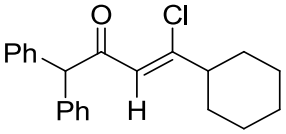
EI-MS: *m/z* 214 (4%, $[M+2]^+$), 212 (12, $[M]^+$), 177 (5), 135 (11), 69 (64), 18 (100). Anal. Calcd. for $C_{12}H_{17}ClO$: C, 67.76; H, 8.06. Found: C, 67.65; H, 7.80.

(*Z*)-3-Chloro-1,3-dicyclohexyl-2-propen-1-one (**3fa**)



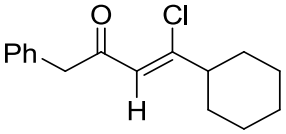
Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 117 mg, 92% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (s, 1H), 2.50 (tt, J = 11.3, 3.6 Hz, 1H), 2.26 (tt, J = 11.3, 3.2 Hz, 1H), 1.93-1.64 (m, 10H), 1.41-1.11 (m, 10H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 202.0, 151.5, 120.7, 51.2, 48.9, 31.3, 28.2, 25.80, 25.77, 25.65, 25.57. IR (neat): 2929.7, 2854.5, 1697.2, 1602.7, 1448.4 cm^{-1}. EI-MS: *m/z* 256 (1%, $[M+2]^+$), 254 (4, $[M]^+$), 219 (20), 171 (100), 135 (41). Anal. Calcd. for $C_{15}H_{23}ClO$: C, 70.71; H, 9.10. Found: C, 70.46; H, 9.23.

(*Z*)-4-Chloro-4-cyclohexyl-1,1-diphenyl-3-buten-2-one (**3ga**)



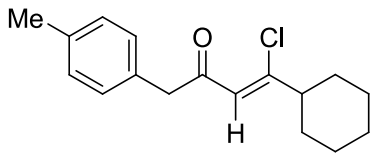
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). White solids, 134 mg, 79% yield: m.p. 104-105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.27 (m, 4H), 7.26-7.20 (m, 6H), 6.34 (s, 1H), 5.20 (s, 1H), 2.18 (tt, J = 11.3, 3.2 Hz, 1H), 1.80-1.70 (m, 4H), 1.68-1.60 (m, 1H), 1.35-1.06 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.8, 153.7, 138.1, 129.1, 128.5, 127.1, 121.2, 64.9, 48.9, 31.0, 25.6, 25.5. IR (KBr): 2933.5, 2848.7, 1701.1, 1604.7, 1110.9, 704.0 cm^{-1}. EI-MS: *m/z* 340 (0.1%, $[M+2]^+$), 338 (0.3, $[M]^+$), 171 (100), 165 (36), 135 (29). Anal. Calcd. for $C_{22}H_{23}ClO$: C, 77.98; H, 6.84. Found: C, 77.96; H, 6.93.

(*Z*)-4-Chloro-4-cyclohexyl-1-phenyl-3-buten-2-one (**3ha**)



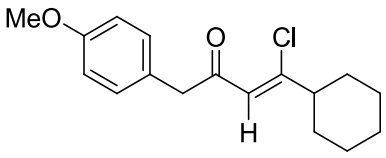
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 117 mg, 89% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.30 (m, 2H), 7.26-7.19 (m, 3H), 6.28 (s, 1H), 3.84 (m, 2H), 2.22 (tt, J = 11.3, 3.2 Hz, 1H), 1.83-1.76 (m, 4H), 1.69-1.65 (m, 1H), 1.39-1.10 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.9, 152.8, 133.9, 129.4, 128.5, 126.9, 121.0, 50.9, 48.9, 31.1, 25.7. 25.5. IR (neat): 2929.7, 2854.5, 1685.7, 1593.1, 1450.4, 1072.3, 696.3 cm^{-1}. EI-MS: *m/z* 264 (0.1%, $[M+2]^+$), 262 (0.3, $[M]^+$), 227 (3), 171 (100), 135 (30). Anal. Calcd. for $C_{16}H_{19}ClO$: C, 73.13; H, 7.29. Found: C, 72.88; H, 7.32.

(*Z*)-4-Chloro-4-cyclohexyl-1-(4-methylphenyl)-3-buten-2-one (**3ia**)



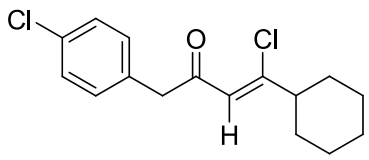
Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 102 mg, 74% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13-7.06 (m, 4H), 6.27 (s, 1H), 3.79 (s, 2H), 2.32 (s, 3H), 2.21 (tt, J = 10.9, 2.7 Hz, 1H), 1.88-1.74 (m, 4H), 1.71-1.63 (m, 1H), 1.38-1.08 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.1, 152.6, 136.4, 130.8, 129.27, 129.23, 121.0, 50.5, 48.8, 31.1, 25.7, 25.5, 20.9. IR (neat): 2929.7, 2854.5, 1697.2, 1602.7, 1514.0, 1450.4 cm^{-1}. EI-MS: *m/z* 278 (0.3%, $[M+2]^+$), 276 (1, $[M]^+$), 241 (13), 171 (100), 135 (46). ESI-HRMS: Calcd. for $C_{17}H_{21}ClONa$ ($[M+Na]^+$), 229.1173. Found, 299.1174.

(*Z*)-4-Chloro-4-cyclohexyl-1-(4-methoxyphenyl)-3-buten-2-one (**3ja**)



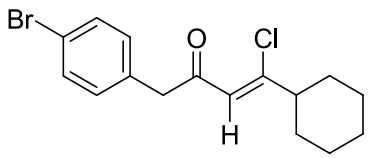
Isolated by column chromatography (silica gel, hexane/AcOEt = 12/1). Pale yellow oil, 93.8 mg, 64% yield: This compound was rather unstable under air and moisture, and turned to black gum in a few days. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 6.27 (s, 1H), 3.78 (s, 3H), 3.77 (s, 2H), 2.22 (tt, J = 11.3, 3.2 Hz, 1H), 1.85-1.77 (m, 4H), 1.70-1.66 (m, 1H), 1.38-1.11 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.3, 158.5, 152.7, 130.5, 125.9, 121.0, 114.0, 55.2, 50.0, 48.9, 31.1, 25.7, 25.6. IR (neat): 2931.6, 2854.5, 1697.2, 1602.7, 1514.0, 1249.8, 1176.5, 1033.8, 831.3 cm^{-1}. EI-MS: *m/z* 294 (1%, $[M+2]^+$), 292 (4, $[M]^+$), 257 (18), 171 (50), 121 (100). ESI-HRMS: Calcd. for $C_{17}H_{21}ClO_2Na$ ($[M+Na]^+$), 315.1122. Found, 315.1125.

(*Z*)-4-Chloro-4-cyclohexyl-1-(4-chlorophenyl)-3-buten-2-one (**3ka**)



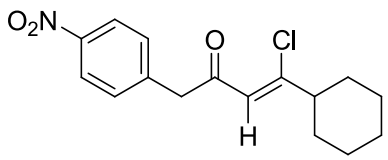
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 113 mg, 76% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 6.27 (s, 1H), 3.83 (s, 2H), 2.24 (tt, J = 11.3, 3.2 Hz, 1H), 1.85-1.78 (m, 4H), 1.70-1.67 (m, 1H), 1.39-1.10 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.3, 153.3, 132.8, 132.4, 130.8, 128.6, 121.1, 49.9, 48.9, 31.1, 25.7, 25.5. IR (neat): 2931.6, 2854.5, 1697.2, 1593.1, 1490.9, 1091.6 cm^{-1}. EI-MS: *m/z* 296 (0.1%, $[M]^+$), 173 (41), 171 (100), 135 (48). ESI-HRMS: Calcd. for $C_{16}H_{18}Cl_2ONa$ ($[M+Na]^+$), 319.0627. Found, 319.0627.

(*Z*)-1-(4-Bromophenyl)-4-chloro-4-cyclohexyl-3-buten-2-one (**3la**)



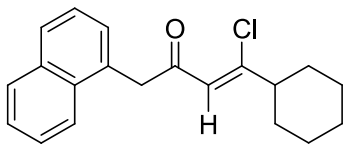
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 150 mg, 88% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 6.27 (s, 1H), 3.81 (s, 2H), 2.24 (tt, J = 10.9, 3.2 Hz, 1H), 1.85-1.78 (m, 4H), 1.70-1.67 (m ,1H), 1.39-1.10 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.21, 153.4, 132.9, 131.6, 131.2, 121.1, 120.9, 50.0, 48.9, 31.1, 25.7, 25.5. IR (neat): 2929.7, 2854.5, 1697.2, 1595.0, 1488.9, 1070.4, 1012.6 cm^{-1}. EI-MS: *m/z* 342 (0.1%, $[M+2]^+$), 173 (43) 171 (100), 135 (36). Anal. Calcd. for $C_{16}H_{18}BrClO$: C, 56.24; H, 5.31. Found: C, 56.01; H, 5.21.

(*Z*)-4-Chloro-4-cyclohexyl-1-(4-nitrophenyl)-3-buten-2-one (**3ma**)



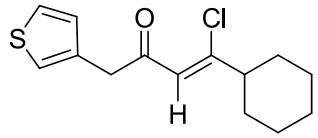
Isolated by column chromatography (silica gel, hexane/AcOEt = 10/1). Pale yellow solids, 79.0 mg, 51% yield: m.p. 60-61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.6 Hz, 2H), 6.33 (s, 1H), 4.03 (s, 2H), 2.32-2.25 (m, 1H), 1.88-1.80 (m, 4H), 1.72-1.69 (m, 1H), 1.41-1.12 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.2, 154.3, 146.9, 141.5, 130.5, 123.6, 121.3, 50.1, 49.1, 31.1, 25.7, 25.5. IR (KBr): 2927.7, 2850.6, 1703.0, 1612.4, 1512.1, 1342.4, 1109.0, 727.1 cm^{-1}. EI-MS: *m/z* 307 (0.1%, $[M]^+$), 173 (29) 171 (78), 135 (41), 18 (100). Anal. Calcd. for $C_{16}H_{18}ClNO_3$: C, 62.44; H, 5.89. Found: C, 62.20; H, 5.95.

(*Z*)-4-Chloro-4-cyclohexyl-1-(1-naphthyl)-3-buten-2-one (**3na**)



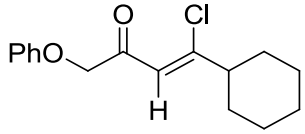
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale brown oil, 119 mg, 76% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.86 (m, 1H), 7.83-7.81 (m, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.50-7.34 (m, 3H), 7.33 (d, J = 6.3 Hz, 1H), 6.27 (s, 1H), 4.23 (s, 2H), 2.13 (tt, J = 11.3, 3.2 Hz, 1H), 1.76-1.65 (m, 4H), 1.65-1.57 (m, 1H), 1.29-1.12 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.0, 153.0, 133.7, 132.2, 130.7, 128.6, 128.1, 127.9, 126.3, 125.7, 125.4, 123.9, 120.6, 48.9, 48.8, 30.9, 25.6, 25.5. IR (neat): 2931.6, 2854.5, 1697.2, 1598.9, 1508.2, 1450.4, 779.2 cm^{-1}. EI-MS: *m/z* 314 (2%, $[M+2]^+$), 312 (7, $[M]^+$) 173 (43), 171 (100), 135 (42). ESI-HRMS: Calcd. for $C_{20}H_{21}ClONa$ ($[M+Na]^+$), 335.1173. Found, 335.1180.

(*Z*)-4-Chloro-4-cyclohexyl-1-(3-thienyl)-3-buten-2-one (**3oa**)



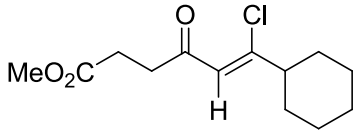
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Yellow oil, 103 mg, 77% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.27 (m, 1H), 7.10-7.07 (m, 1H), 6.97 (d, J = 5.0 Hz, 1H), 6.29 (s, 1H), 3.87 (s, 2H), 2.24 (tt, J = 11.9, 2.7 Hz, 1H), 1.86-1.77 (m, 4H), 1.70-1.67 (m, 1H), 1.38-1.00 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.4, 152.9, 133.6, 128.5, 125.7, 122.9, 120.9, 48.9, 45.2, 31.1, 25.7, 25.5. IR (neat): 2931.6, 2854.5, 1697.2, 1602.7, 1450.4, 734.8 cm^{-1}. EI-MS: *m/z* 270 (4%, $[M+2]^+$), 268 (15, $[M]^+$) 173 (45), 171 (100), 135 (50). Anal. Calcd. for $C_{14}H_{17}ClOS$: C, 62.56; H, 6.37. Found: C, 62.31; H, 6.27.

(*Z*)-4-Chloro-4-cyclohexyl-1-phenoxy-3-buten-2-one (**3pa**)



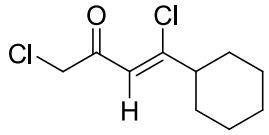
Isolated by column chromatography (silica gel, hexane/AcOEt = 12/1). Pale yellow oil, 115 mg, 82% yield: This compound was rather unstable under air and moisture, and turned to black gum in a few days. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.25 (m, 2H), 7.00 (dt, J = 7.2, 1.4 Hz, 1H), 6.90-6.84 (m, 2H), 6.57 (s, 1H), 4.70 (s, 2H), 2.30 (tt, J = 10.9, 3.2 Hz, 1H), 1.90-1.77 (m, 4H), 1.73-1.67 (m, 1H), 1.41-1.10 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.2, 157.7, 155.5, 129.5, 121.5, 118.3, 114.5, 73.1, 49.2, 31.1, 25.7, 25.5. IR (neat): 2931.6, 2854.5, 1697.2, 1596.9, 1496.7, 754.1 cm^{-1}. EI-MS: *m/z* 280 (4%, $[M+2]^+$), 278 (16, $[M]^+$) 243 (17), 171 (100), 135 (59), 77 (78). ESI-HRMS: Calcd. for $C_{16}H_{19}ClO_2Na$ ($[M+Na]^+$), 301.0966. Found, 301.0965.

(*Z*)-6-Chloro-6-cyclohexyl-4-oxo-6-hexenoic acid methy ester (**3qa**)



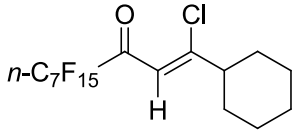
Isolated by column chromatography (silica gel, hexane/AcOEt = 8/1). Pale yellow oil, 110 mg, 85% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.29 (s, 1H), 3.68 (s, 3H), 2.96 (t, J = 6.8 Hz, 2H), 2.63 (t, J = 6.8 Hz, 2H), 2.28 (tt, J = 11.3, 3.2 Hz, 1H), 1.93-1.87 (m, 2H), 1.86-1.79 (m, 2H), 1.74-1.68 (m, 1H), 1.42-1.03 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.8, 173.2, 152.7, 122.0, 51.8, 49.1, 38.7, 31.3, 27.8, 25.9, 25.7. IR (neat): 2931.6, 2856.4, 1739.7, 1701.1, 1666.4, 1608.5, 1436.9, 1211.2, 1164.9 cm^{-1}. EI-MS: *m/z* 260 (0.1%, $[M+2]^+$), 258 (0.2, $[M]^+$), 173 (42), 171 (100), 135 (46). Anal. Calcd. for $C_{13}H_{19}ClO_3$: C, 60.35; H, 7.40. Found: C, 60.48; H, 7.51.

(*Z*)-1,4-Dichloro-4-cyclohexyl-3-buten-2-one (**3ra**)[17]



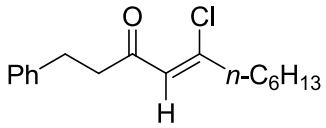
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 108 mg, 98% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.49 (s, 1H), 4.28 (s, 2H), 2.34 (tt, J = 11.3, 3.2 Hz, 1H), 1.94-1.87 (m, 2H), 1.86-1.80 (m, 2H), 1.75-1.67 (m, 1H), 1.46-1.13 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.6, 156.1, 118.8, 49.23, 49.18, 31.1, 25.7, 25.5. IR (neat): 2931.6, 2854.5, 1697.2, 1604.7, 1450.4 cm^{-1}. EI-MS: *m/z* 222 (0.1%, $[M+2]^+$), 220 (0.1, $[M]^+$), 173 (44) 171 (100), 135 (36), 79 (43).

(*Z*)-1-Chloro-1-cyclohexyl-4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-pentadecafluoro-1-decen-3-one (**3sa**)



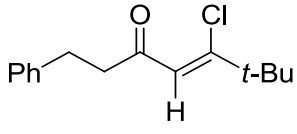
Isolated by column chromatography (silica gel, hexane/AcOEt = 50/1). Colorless oil, 185 mg, 68% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.71 (s, 1H), 2.44 (tt, J = 11.3, 3.6 Hz, 1H), 1.96-1.83 (m, 4H), 1.77-1.70 (m, 1H), 1.51-1.15 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 179.0 (t, $^2J_{C\text{-}F}$ = 24.8 Hz), 165.1, 121.4-108.1 (m, *n*-C_7F_{15}), 113.7, 50.3, 31.3, 25.7, 25.5. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ –80.9, –120.9, –121.5, –122.09, –122.16, –122.8, –126.3. IR (neat): 2937.4, 2862.2, 1718.5, 1596.9, 1242.1, 1211.2, 1149.5 cm^{-1}. EI-MS: *m/z* 542 (2%, $[M+2]^+$), 541 (1, $[M+1]^+$), 540 (6, $[M]^+$), 505 (8), 485 (24), 173 (86), 171 (100). Anal. Calcd. for $C_{16}H_{12}ClF_{15}O$: C, 35.54; H, 2.24. Found: C, 35.54; H, 2.27.

(*Z*)-5-Chloro-1-phenyl-4-undecen-3-one (**3ab**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 120 mg, 86% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.24 (m, 2H), 7.22-7.15 (m, 3H), 6.23 (s, 1H), 2.93 (m, 4H), 2.00 (t, J = 7.7 Hz, 2H), 1.65-1.54 (m, 2H), 1.35-1.23 (m, 6H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.6, 147.3, 141.0, 128.37, 128.30, 126.0, 123.9, 45.5, 41.3, 31.6, 29.7, 28.1, 27.1, 22.4, 13.9. IR (neat): 2929.7, 2858.3, 1701.1, 1608.5, 1454.2, 698.2 cm^{-1}. EI-MS: *m/z* 280 (0.5%, $[M+2]^+$), 278 (2, $[M]^+$), 243 (100), 173 (31), 105 (35). ESI-HRMS: Calcd. for $C_{17}H_{23}ClONa$ ($[M+Na]^+$), 301.1330. Found, 301.1331.

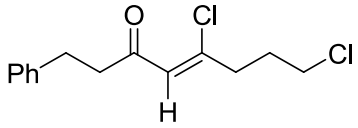
(*Z*)-5-Chloro-6,6-dimethyl-1-phenyl-4-hepten-3-one (**3ac**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 112 mg, 89% yield: ^{1}H NMR (400

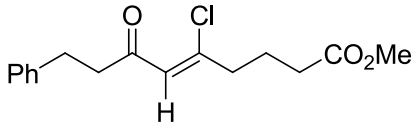
MHz, $CDCl_3$): δ 7.29-7.24 (m, 2H), 7.21-7.15 (m, 3H), 6.24 (s, 1H), 2.94 (m, 4H), 1.21 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 198.9, 155.1, 140.9, 128.33, 128.28, 125.9, 121.4, 45.6, 39.9, 29.8, 28.5. IR (neat): 2970.2, 1703.0, 1602.7, 1456.2, 1097.4, 700.1 cm^{-1}. EI-MS: *m/z* 252 (1%, $[M+2]^+$), 250 (3, $[M]^+$), 215 (74), 193 (44), 145 (53), 109 (100). Anal. Calcd. for $C_{15}H_{19}ClO$: C, 71.84; H, 7.64. Found: C, 71.73; H, 7.76.

(*Z*)-5,8-Dichloro-1-phenyl-4-octen-3-one (**3ad**)



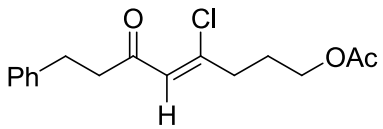
Isolated by column chromatography (silica gel, hexane/AcOEt = 15/1). Colorless oil, 105 mg, 77% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.24 (m, 2H), 7.22-7.16 (m, 3H), 6.31 (s, 1H), 3.52 (t, J = 6.3 Hz, 2H), 2.95-2.89 (m, 4H), 2.59 (t, J = 7.2 Hz, 2H), 2.11-2.02 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.2, 144.7, 140.8, 128.35, 128.26, 126.0, 124.9, 45.5, 43.2, 38.1, 29.62, 29.55. IR (neat): 2958.6, 1699.2, 1614.3, 1456.2, 1118.6, 700.1 cm^{-1}. EI-MS: *m/z* 272 (0.5%, $[M+2]^+$), 270 (2, $[M]^+$), 237 (26), 235 (88), 165 (65), 91 (84), 18 (100). Anal. Calcd. for $C_{14}H_{16}Cl_2O$: C, 62.01; H, 5.95. Found: C, 61.88; H, 5.97.

(*Z*)-5-Chloro-7-oxo-9-phenyl-5-nonenoic acid methy ester (**3ae**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 5/1). Colorless oil, 112 mg, 76% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.24 (m, 2H), 7.21-7.15 (m, 3H), 6.26 (s, 1H), 3.66 (s, 3H), 2.95-2.90 (m, 4H), 2.46 (t, J = 7.2 Hz, 2H), 2.33 (t, J = 7.2 Hz, 2H), 1.92 (quintet, J = 7.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.3, 173.0, 145.5, 140.8, 128.3, 128.2, 125.9, 124.5, 51.5, 45.4, 40.1, 32.2, 29.6, 22.2. IR (neat): 2950.9, 1733.9, 1697.2, 1616.2, 1456.2, 700.1 cm^{-1}. EI-MS: *m/z* 296 (0.1%, $[M+2]^+$), 294 (0.3, $[M]^+$), 259 (89), 227 (24), 105 (76), 91 (100). Anal. Calcd. for $C_{16}H_{19}ClO_3$: C, 65.19; H, 6.50. Found: C, 65.05; H, 6.25.

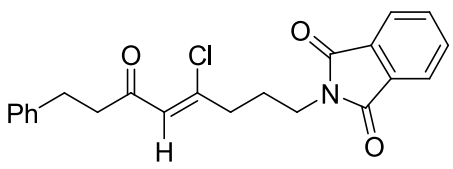
(*Z*)-8-Acetyloxy-5-chloro-1-phenyl-4-octen-3-one (**3af**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 5/1). Colorless oil, 117 mg, 79% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.24 (m, 2H), 7.21-7.15 (m, 3H), 6.28 (s, 1H), 4.08 (t, J = 6.3 Hz, 2H), 2.95-2.90 (m, 4H), 2.45 (t, J = 7.7 Hz, 2H), 2.04 (s, 3H), 1.99-1.91 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.2, 170.7, 145.3, 140.8, 128.3, 128.2, 125.9, 124.4, 62.6, 45.4, 37.7, 29.6, 26.2, 20.7. IR (neat): 2958.6, 1733.9, 1697.2, 1238.2, 1047.3, 700.1 cm^{-1}. EI-MS: *m/z* 294 (0.1%,

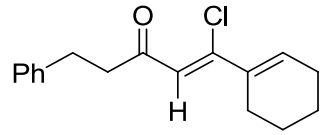
[M]$^+$), 259 (24), 199 (17), 105 (24), 91 (49), 18 (100). Anal. Calcd. for $C_{16}H_{19}ClO_3$: C, 65.19; H, 6.50. Found: C, 65.38; H, 6.57.

(*Z*)-2-(4-Chloro-6-oxo-8-phenyl-4-octenyl)-*1H*-isoindole-1,3(*2H*)-dione (**3ag**)



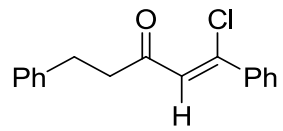
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). Colorless oil, 160 mg, 84% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.80 (m, 2H), 7.73-7.67 (m, 2H), 7.31-7.22 (m, 2H), 7.22-7.12 (m, 3H), 6.34 (s, 1H), 3.71 (t, J = 6.8 Hz, 2H), 2.95-2.86 (m, 4H), 2.48 (t, J = 7.2 Hz, 2H), 2.02 (quintet, J = 7.2 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.2, 168.1, 145.0, 140.8, 133.9, 131.7, 128.27, 128.21, 125.9, 124.4, 123.1, 45.4, 38.4, 36.6, 29.6, 26.0. IR (neat): 2935.4, 1770.5, 1714.6, 1616.2, 1396.4, 721.3 cm^{-1}. EI-MS: *m/z* 346 (20%, [M–Cl]$^+$), 160 (34), 91 (24), 18 (100). ESI-HRMS: Calcd. for $C_{22}H_{20}ClNO_3Na$ ([M+Na]$^+$), 404.1024. Found, 404.1011.

(*Z*)-1-Chloro-1-cyclohexenyl-5-phenyl-1-penten-3-one (**3ah**)



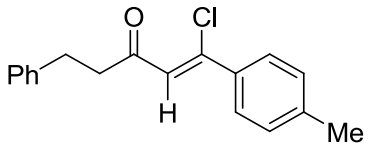
Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 109 mg, 80% yield: This compound was rather unstable under air and moisture, and turned to black gum in a few days. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.23 (m, 2H), 7.23-7.16 (m, 3H), 6.78-6.73 (m, 1H), 6.33 (s, 1H), 2.97 (m, 4H), 2.29-2.15 m, (4H), 1.74-1.66 (m, 2H), 1.64-1.54 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.5, 143.3, 141.0, 136.2, 133.4, 128.34, 128.29, 125.9, 120.3, 46.0, 29.9, 26.25, 26.22, 22.3, 21.4. IR (neat): 2937.4, 1697.2, 1456.2, 731.0, 700.1 cm^{-1}. EI-MS: *m/z* 276 (1%, [M+2]$^+$), 274 (4, [M]$^+$), 239 (88), 169 (37), 105 (50), 91 (100). ESI-HRMS: Calcd. for $C_{17}H_{19}ClONa$ ([M+Na]$^+$), 297.1022. Found, 297.1019.

(*Z*)-1-Chloro-1,5-diphenyl-1-penten-3-one (**3ai**)



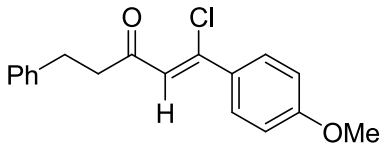
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 110 mg, 81% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, J = 7.7, 1.8 Hz, 2H), 7.32-7.09 (m, 8H), 6.68 (s, 1H), 2.95-2.86 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.1, 142.3, 140.9, 137.0, 130.6, 128.5, 128.39, 128.33, 127.2, 126.0, 123.5, 45.8, 29.8. IR (neat): 3026.1, 2358.8, 1697.2, 1589.2, 1490.9, 758.0, 696.3 cm^{-1}. EI-MS: *m/z* 272 (0.5%, [M+2]$^+$), 270 ([M]$^+$, 1), 269 ([M–1]$^+$, 3) 235 (35), 165 (58), 91 (100). Anal. Calcd. for $C_{17}H_{15}ClO$: C, 75.41; H, 5.58. Found: C, 75.69; H, 5.74.

(*Z*)-1-Chloro-1-(4-methylphenyl)-5-phenyl-1-penten-3-one (**3aj**)



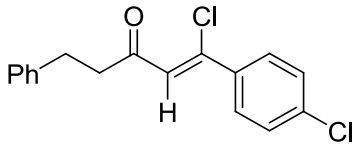
Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 125 mg, 88% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 8.2 Hz, 2H), 7.29-7.15 (m, 7H), 6.73 (s, 1H), 3.03-2.95 (m, 4H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.4, 142.9, 141.1, 140.9, 134.3, 129.2, 128.34, 128.27, 127.1, 125.9, 122.6, 45.9, 29.8, 21.1. IR (neat): 3028.0, 1697.2, 1587.3, 1508.2, 1091.6, 812.0, 700.1 cm^{-1}. EI-MS: *m/z* 284 (0.1%, $[M]^+$), 250 (19), 249 (70), 179 (34), 115 (25), 18 (100). Anal. Calcd. for $C_{18}H_{17}ClO$: C, 75.92; H, 6.02. Found: C, 75.85; H, 6.26.

(*Z*)-1-Chloro-1-(4-methoxyphenyl)-5-phenyl-1-penten-3-one (**3ak**)



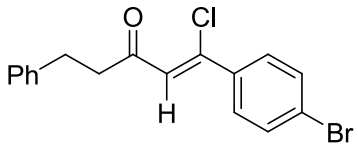
Isolated by column chromatography (silica gel, hexane/AcOEt = 15/1). Colorless oil, 121 mg, 81% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 9.1 Hz, 2H), 7.30-7.14 (m, 5H), 6.88 (d, J = 8.6 Hz, 2H), 6.70 (s, 1H), 3.80 (s, 3H), 3.05-2.94 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.4, 161.6, 142.8, 140.9, 129.3, 128.8, 128.36, 128.30, 128.9, 121.6, 113.8, 55.3, 45.9, 29.9. IR (neat): 2931.6, 1695.3, 1568.0, 1508.2, 1456.2, 1257.5, 1178.4, 1091.6, 1031.8, 829.3, 700.1 cm^{-1}. EI-MS: *m/z* 302 (0.1%, $[M+2]^+$), 300 (0.3, $[M]^+$), 265 (100), 197 (17), 195 (52), 18 (97). ESI-HRMS: Calcd. for $C_{18}H_{17}ClO_2Na$ ($[M+Na]^+$), 323.0809. Found, 323.0816.

(*Z*)-1-Chloro-1-(4-chlorophenyl)-5-phenyl-1-penten-3-one (**3al**)



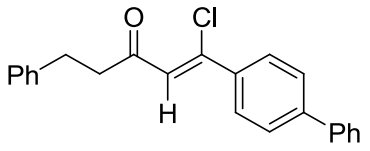
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 115 mg, 75% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.53 (m, 2H), 7.37-7.32 (m, 2H), 7.31-7.25 (m, 2H), 7.23-7.16 (m, 3H), 6.72 (s, 1H), 3.06-2.95 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 194.3, 141.3, 140.7, 136.7, 135.6, 128.8, 128.45, 128.42, 128.31, 126.1, 123.8, 45.9, 29.8. IR (neat): 1697.2, 1589.2, 1488.9, 1089.7, 1012.5, 823.5, 700.1 cm^{-1}. EI-MS: *m/z* 303 (0.1%, $[M-1]^+$), 271 (29), 269 (100), 201 (23), 199 (39), 136 (28), 91 (35), 18 (100). ESI-HRMS: Calcd. for $C_{17}H_{14}Cl_2ONa$ ($[M+Na]^+$), 327.0314. Found, 327.0321.

(*Z*)-1-(4-Bromophenyl)-1-chloro-5-phenyl-1-penten-3-one (**3am**)



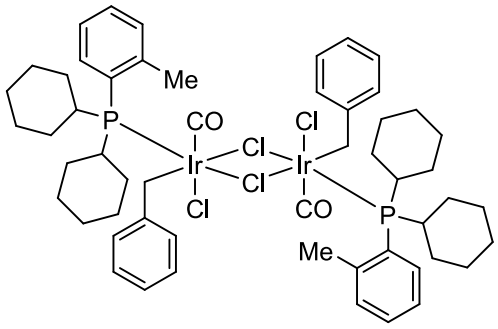
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow oil, 102 mg, 58% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.46 (m, 4H), 7.30-7.16 (m, 5H), 6.72 (s, 1H), 3.05-2.95 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.3, 141.4, 140.7, 136.0, 131.7, 128.6, 128.4, 128.3, 126.1, 125.1, 123.8, 45.9, 29.8. IR (neat): 1697.2, 1587.3, 1485.1, 1072.3, 1008.7, 819.7, 732.9, 700.1 cm^{-1}. EI-MS: *m/z* 347 (0.1%, $[M-1]^+$), 315 (43), 313 (47), 245 (31), 164 (28), 91 (51), 18 (100). Anal. Calcd. for $C_{17}H_{14}BrClO$: C, 58.40; H,4.04. Found: C, 58.13; H, 4.15.

(*Z*)-1-(4-Biphenyl)-1-chloro-5-phenyl-1-penten-3-one (**3an**)



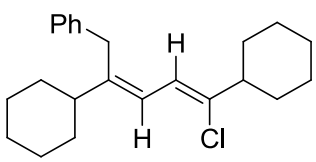
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Pale yellow solids, 135 mg, 78% yield: m.p. 78-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.6 Hz, 2H), 7.60-7.54 (m, 4H), 7.45-7.40 (m, 2H), 7.38-7.15 (m, 6H), 6.78 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.5, 143.4, 142.4, 140.9, 139.5, 135.8, 128.8, 128.40, 128.32, 127.9, 127.7, 127.1, 127.0, 126.0, 123.2, 46.9, 29.8. IR (KBr): 1685.7, 1577.7, 1541.0, 763.8, 690.5 cm^{-1}. EI-MS: *m/z* 346 (0.1%, $[M]^+$), 311 (18), 205 (6), 178 (14), 105 (3), 91 (7), 18 (100). Anal. Calcd. for $C_{23}H_{19}ClO$: C, 79.64; H, 5.52. Found: C, 79.89; H, 5.50.

$[IrCl_2(CO)\{PCy_2(o\text{-tol})\}(CH_2Ph)]_2$ (**4**)



White solids, 54.6 mg, 81% yield: m.p. > 250 °C (decomp.). The solubility of **4** in common organic solvent was not enough to obtain clear-cut NMR data. IR (KBr): 2933.5, 2850.6, 2054.0, 1450.4 cm^{-1}. ESI-HRMS: Calcd. for $C_{54}H_{72}Cl_4Ir_2O_2P_2$ ($[M-Cl]^+$), 1305.3326. Found, 1305.3311. Anal. Calcd. for $C_{54}H_{72}Cl_4OIr_2O_2P_2$: C, 48.35; H, 5.41. Found: C, 48.77; H, 5.35.

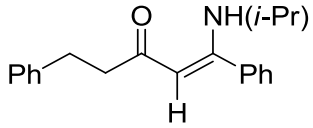
(*Z*,*E*)-1-Chloro-1,4-dicyclohexyl-5-phenyl-1,3-pentadiene (**5**)



Isolated by column chromatography (silica gel, hexane) followed by GPC. Colorless oil, 7.0 mg, 41% yield (containing some unidentified isomers): ^{1}H NMR (400 MHz,

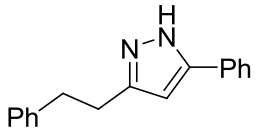
$CDCl_3$): δ 7.26-7.21 (m, 2H), 7.18-7.15 (m, 3H), 5.84 (s, 1H), 5.21 (d, J = 9.6 Hz, 1H), 3.46 (s, 2H), 2.21-2.00 (m, 2H), 1.82-0.99 (m, 20H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 140.21, 139.3, 136.5, 132.4, 128.9, 128.0, 125.8, 121.3, 47.5, 43.0, 38.3, 32.7, 31.6, 26.09, 26.04, 25.98, 25.91. EI-MS: *m/z* 344 (14%, $[M+2]^+$), 343 (11, $[M+1]^+$), 342 ($[M]^+$, 40), 324 (33), 307 (92), 91 (100). EI-HRMS: Calcd. for $C_{23}H_{31}Cl$ ($[M]^+$), 342.2109. Found, 342.2111.

(*Z*)-1-Isopropylamino-1,5-diphenyl-1-penten-3-one (**6**)



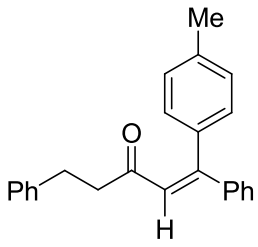
Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1 then 10/1). Pale yellow oil, 66.7 mg, 76% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 10.74 (*d*, J = 9.1 Hz, 1H), 7.41-7.37 (m, 3H), 7.34-7.14 (m, 7H), 4.98 (s, 1H), 3.62-349 (m, 1H), 2.98-2.94 (m, 2H), 2.64-2.60 (m, 2H), 1.14 (d, J = 6.4 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 196.9, 164.4, 141.9, 135.8, 129.1, 128.3, 128.25, 128.23, 127.3, 125.6, 95.9, 45.8, 43.7, 31.8, 24.1. IR (KBr): 2972.1, 1606.6, 1568.0, 1483.2, 1315.4, 1114.8, 700.1 cm^{-1}. EI-MS: *m/z* 294 (7%, $[M+1]^+$), 293 (46, $[M]^+$), 202 (11), 188 (100), 160 (70), 103 (22). ESI-HRMS: Calcd. for $C_{20}H_{24}ON$ ($[M]^+$), 294.1852. Found, 294.1850.

5-Phenyl-3-(2-phenylethyl)-*1H*-pyrazole (**7**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1 then 1/1). Pale yellow solids, 38.0 mg, 51% yield: m.p. 75-76 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 9.83 (br, 1H), 7.69 (d, J = 6.8 Hz, 2H), 7.36-7.32 (m, 2H), 7.29-7.22 (m, 3H), 7.21-7.17 (m, 1H), 7.13-7.11 (m, 2H), 6.34 (s, 1H), 2.93 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.4, 147.4, 140.9, 132.2, 128.7, 128.4, 128.3, 127.9, 126.2, 125.7, 101.3, 35.4, 28.3. IR (KBr): 3240.2, 765.7, 694.3 cm^{-1}. EI-MS: *m/z* 249 (11%, $[M+1]^+$), 248 (69, $[M]^+$), 157 (100), 128 (43), 91 (92), 77 (31). ESI-HRMS: Calcd. for $C_{17}H_{17}N_2$ ($[M+H]^+$), 249.1386. Found, 249.1375.

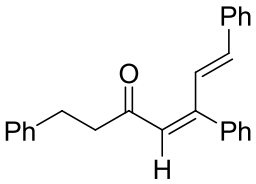
(*Z*)-1-(4-Methylphenyl)-1,5-diphenyl-1-penten-3-one (**8**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 25/1). Pale yellow oil, 87.8 mg, 90% yield (*Z*/*E* = 93:7): ^1H NMR (400 MHz, $CDCl_3$): δ 7.38-7.11 (m, 10H), 7.06-7.00 (m, 4H), 6.59 (minor, (*E*)-isomer, s, 1H), 6.49 (major, (*Z*)-isomer, s, 1H), 2.80 (t, J = 7.7 Hz, 2H), 2.54 (t, J = 7.7 Hz, 2H), 2.38 (major,

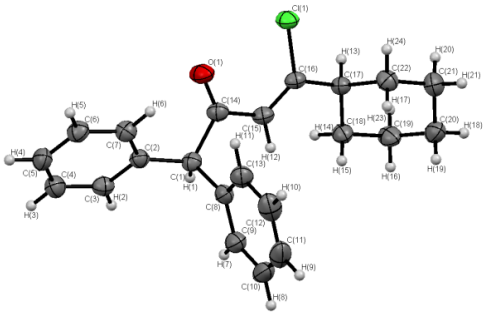
(*Z*)-isomer, s, 1H), 2.32 (minor, (*E*)-isomer, s, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 201.4, 153.6, 141.0, 138.5, 135.9, 129.5, 129.2, 128.9, 128.4, 128.20, 128.17, 126.3, 125.8, 44.4, 30.3, 21.2. IR (KBr): 3026.1, 2922.0, 1689.5, 1660.6, 1593.1, 1494.7, 1446.5, 1353.9, 698.2 cm^{-1}. EI-MS: *m/z* 327 (2%, $[M+1]^+$), 326 (9, $[M]^+$), 311 (7), 234 (28), 221 (100), 194 (23), 178 (26), 115 (22). Anal. Calcd. for $C_{24}H_{22}O$: C, 88.31; H, 6.79. Found: C, 88.12; H, 6.85.

(*Z*,*E*)-1,5,7-Triphenyl-4,6-heptadien-3-one (**9**)

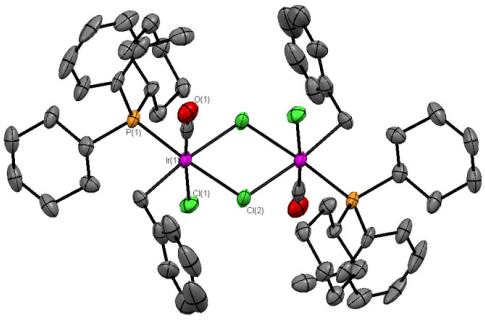


Isolated by column chromatography (silica gel, hexane/AcOEt = 20/1). Yellow oil, 68.4 mg, 67% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 16.3 Hz, 1H), 7.49-7.47 (m, 2H), 7.42-7.13 (m, 13H), 6.66 (d, J = 16.3 Hz, 1H), 6.11 (s, 1H), 3.02-2.98 (m, 2H), 2.90-2.85 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 199.8, 154.2, 141.2, 141.0, 140.0, 136.5, 129.0, 128.9, 128.61, 128.56, 128.4, 128.3, 128.2, 127.6, 126.6, 125.9, 124.4, 46.4, 30.2. IR (KBr): 3060.8, 3026.1, 1672.2, 1608.5, 1556.4, 1488.9, 1448.9, 1097.4, 732.9 cm^{-1}. EI-MS: *m/z* 339 (3%, $[M+1]^+$), 338 (16, $[M]^+$), 247 (75), 233 (100), 203 (53), 190 (26), 127 (28). ESI-HRMS: Calcd. for $C_{25}H_{23}O$ ($[M+H]^+$), 339.1743. Found, 339.1752.

X-ray Diffraction Studies of 3ga and 4



Single crystal of **3ga** was obtained by recrystallization from CH_2Cl_2/hexane solution. Crystal data for **3ga**: $C_{22}H_{23}ClO$, M = 338.88, monoclinic, space group = $P2_1/n$ (#14), a = 6.157(2) Å, b = 18.186(7) Å, c = 16.126(6) Å, β = 90.867(5)°, V = 1805.5(12) $Å^3$, Z = 4, density (calc.) = 1.247, total reflections collected = 13300, unique reflections = 4018 (R_{int} = 0.042), GOF = 1.003 The final $R1$ factor was 0.0556 ($I>2\sigma(I)$) ($wR2$ = 0.1724, all data).



Single crystal of **4** was obtained by recrystallization from CH_2Cl_2/hexane solution. Crystal data for **4**: $C_{27.50}H_{36}Cl_3IrOP$, M = 712.14, monoclinic, space group = P_1 (#2), a = 10.5512(9) Å, b = 12.6165(10) Å, c = 13.1580(14) Å, α = 109.582(2)°, β =

90.867(5)°, γ = 105.0630(9)°, V = 1489.1(2) Å^3, Z = 2, density (calc.) = 1.588, total reflections collected = 11068, unique reflections = 6402 (R_{int} = 0.044), GOF = 1.003 The final $R1$ factor was 0.0523 ($I>2\sigma(I)$) ($wR2$ = 0.1548, all data).

3-5. References and Notes

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(7) The solubility of **4** in common organic solvent was not enough to obtain clear-cut NMR data. The structure and purity of **4** was confirmed by X-ray diffraction study and elementary analysis, respectively.

(8) In the rhodium-catalyzed system, similar mechanism about insertion of terminal alkynes into rhodium-chloro bond has been reported, see: Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941–6946.

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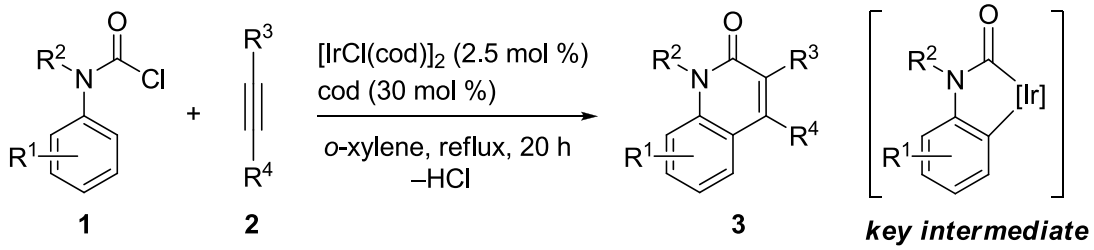
Chapter 4

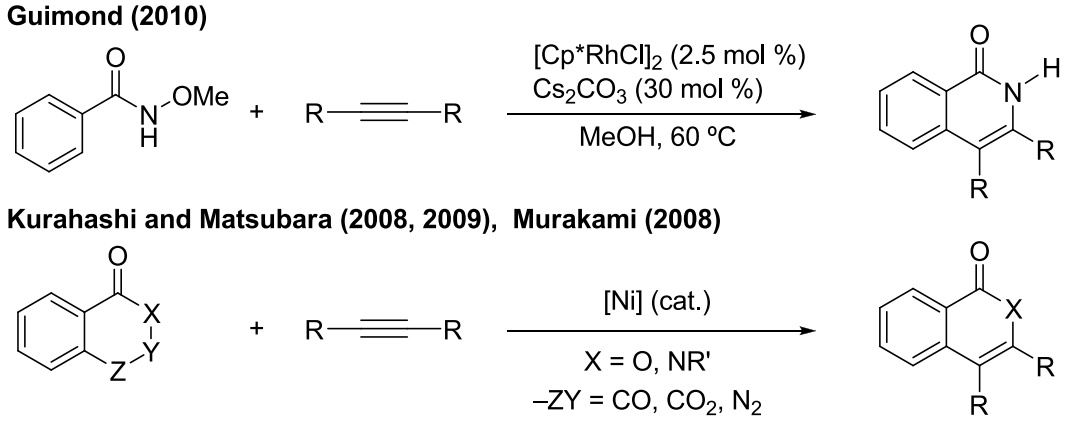
Iridium-Catalyzed Annulation of *N*-Arylcarbamoyl Chlorides with Internal Alkynes

An iridium complex successfully catalyzes the annulations of various *N*-arylcarbamoyl chlorides with internal alkynes to afford 2-quinolones in good to excellent yields. The present reaction is widely applicable to substrates with various functionalities. An amide-iridacycle complex was isolated, and it is likely that such an iridacycle species is a key intermediate in the catalytic reaction.



4-1. Introduction

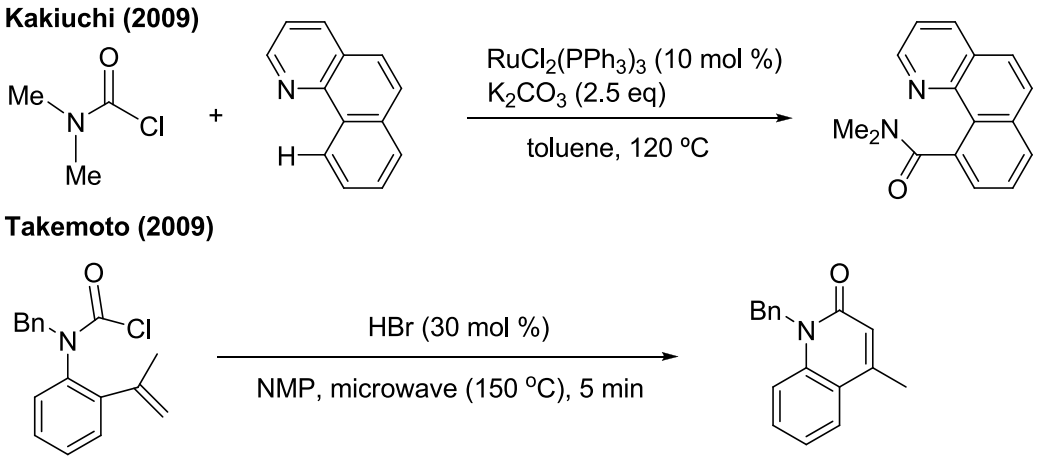
The large number of carbonyl-containing *N*-heterocycles in biologically active molecules have motivated many efforts for their synthesis and functionalization.[1] The transition-metal-catalyzed intermolecular reaction of carbonyl precursors with alkynes is one of the most straightforward methods for constructing cyclic carbonyl compounds.[2-4] For example, Guimond and co-workers reported that the rhodium-catalyzed annulation of benzhydroxamic acids with alkynes giving isoquinolones (Scheme 4-1).[2a] Recently, syntheses of carbonyl-containing heterocycles from alkynes and cyclic precursors along with the elimination of carbon monoxide,[3a,b] carbon dioxide,[3d] and nitrogen[3c] have been reported.



Scheme 4-1. Several synthetic methods for carbonyl-containing *N*-heterocycles.

On the other hand, carbamoyl chlorides are useful substrates for introducing amide functionality in organic synthesis, and they are mainly utilized in transition-metal-catalyzed reactions as coupling reagents.[5] For example, Kakiuchi and co-workers reported the ruthenium-catalyzed aminocarbonylations with carbamoyl chlorides via aromatic C–H bond cleavage (Scheme 4-2).[5b] Recently, Takemoto and co-workers reported the intramolecular cyclization of carbamoyl chlorides with alkenes in the presence of a catalytic amount of HBr.[6] The author considered that *N*-arylcarbamoyl chloride, in particular, would be a promising substrate for providing 2-quinolones[7,8] via transition-metal-catalyzed annulation with alkynes. To realize this transformation, facile decarbonylation[9,10] from the putative acylmetal species must be suppressed in the catalysis. Recently, the author reported the iridium-catalyzed addition of acid chlorides to alkynes (Chapters 2 and 3).[11a] In addition, his research group reported the palladium-catalyzed addition of formamides to alkynes[11b] by suppressing the decarbonylation. In this Chapter, the author demonstrated the annulation of

N-arylcarbamoyl chlorides with internal alkynes to afford 2-quinolones efficiently in the presence of an iridium complex.

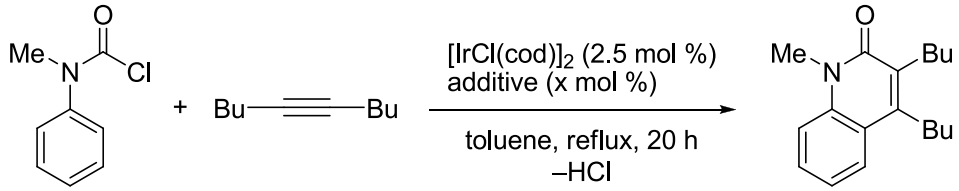


Scheme 4-2. Synthetic methods using carbamoyl chlorides as the substrates.

4-2. Results and Discussion

For the reaction optimization, a reaction of *N*-methyl-*N*-phenylcarbamoyl chloride (**1a**) with 5-decyne (**2a**) was carried out employing various additives with a catalytic amount of $[IrCl(cod)]_2$ in refluxing toluene (Table 4-1). Without an additive, the reaction of **1a** with **2a** afforded 3,4-dibutyl-1-methyl-2-quinolone (**3aa**) in low yield (entry 1). An addition of monodentate phosphines such as PPh_3 and PCy_3 improved the yields of **3aa** moderately (entries 2 and 4). With excess PPh_3 (P/Ir = 2), the yield decreased to 25% (entry 3), while **3aa** was obtained in good yields in refluxing *o*-xylene (entries 1–4). With *rac*-BINAP and IMes, **3aa** was obtained in low yields (entries 5 and 6). Addition of bases to scavenge the evolved HCl did not affect the reaction at all (entries 7–12). 1,5-Cyclooctadiene was found to be an effective additive, giving **3aa** in 82% yield (entries 13–17). In refluxing *o*-xylene, the reaction proceeded smoothly to afford **3aa** quantitatively in the presence of 30 mol % of cod (entry 16). Other dienes, alkenes and a combination of PPh_3 with cod were not effective in the reaction (entries 18–21). Using $[RhCl(cod)]_2$ as a catalyst precursor, **3aa** was not obtained under the reaction conditions examined (entry 22).

Table 4-1. Optimization for the iridium-catalyzed reaction of *N*-methyl-*N*-phenylcarbamoyl chloride (**1a**) with 5-decyne (**2a**).[a]



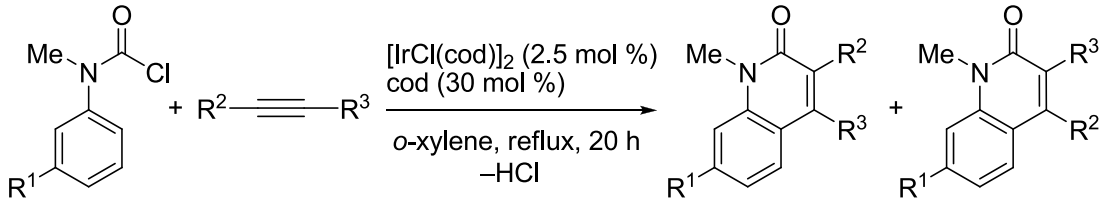
1a **2a** **3aa**

entry	additive (x mol %)	**3aa** % yield[b]
1	none	27 (65)[c]
2	PPh_3 (5)	52 (74)[c]
3	PPh_3 (10)	25 (86)[c]
4	PCy_3 (5)	34 (75)[c]
5	*rac*-BINAP (5)	<1
6	IMes·HCl (5) / KO^{t}Bu (5)	6
7	PPh_3 (5) / $NaHCO_3$ (100)	51
8	PPh_3 (5) / Na_2CO_3 (100)	42
9	PPh_3 (5) / K_2CO_3 (100)	17
10	PPh_3 (5) / KF (100)	40
11	PPh_3 (5) / N(*i*-Pr)$_2$Et (100)	<1
12	PPh_3 (5) / pyridine (100)	<1
13	1,5-cyclooctadiene (5)	65
14	1,5-cyclooctadiene (10)	70
15	1,5-cyclooctadiene (20)	76
16	1,5-cyclooctadiene (30)	82 (92)[c]
17	1,5-cyclooctadiene (50)	80
18	norbornadiene (30)	21
19	dibenzylideneacetone (30)	50
20	cyclooctene (30)	49
21	PPh_3 (5) / 1,5-cyclooctadiene (30)	67
22	1,5-cyclooctadiene (30)	<1[d]

[a] Conditions: *N*-methyl-*N*-phenylcarbamoyl chloride (**1a**) (0.50 mmol), 5-decyne (**2a**) (1.0 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), additive (0–0.50 mmol, 0–100 mol %), in refluxing toluene (1.0 mL), for 20 h. [b] Yields were determined by GC analysis. [c] In refluxing *o*-xylene (1.0 mL). [d] $[RhCl(cod)]_2$ (0.0125 mmol, 2.5 mol %) was used as the catalyst.

Various aliphatic and aromatic internal alkynes (**2b**–**i**) afforded the corresponding 2-quinolones. Importantly, no indole derivatives produced by decarbonylation were obtained during the reaction. 1,4-Dimethoxy-2-butyne (**2b**) and diphenylacetylene (**2c**) reacted with **1a** to give **3ab** and **3ac**, respectively, in good yields (entries 2 and 3). Diarylalkynes **2c**–**e** successfully reacted with *N*-(3-methoxyphenyl)-*N*-methylcarbamoyl chloride (**1b**) to give **3bc**–**be** in high yields, notably as single regioisomers (entries 4–6). Unsymmetrical alkynes 1-cyclohexyl-1-propyne (**2f**) and 1-phenyl-1-propyne (**2g**) reacted smoothly with **1a** to afford **3af** and **3ag**, respectively, in high yields, albeit with low regioselectivities (entries 7 and 8). The use of unsymmetrical alkynes bearing an ether functionality (**2h** and **2i**) improved the regioselectivity of the products (**3ah** and **3ai**), possibly as a result of the directing effect of the oxygen atom (entries 9 and 10). Terminal alkynes such as 1-decyne and phenylacetylene did not afford **3** due to easy oligomerization of substrates under the conditions.

Table 4-2. Iridium-catalyzed reaction of *N*-arylcarbamoyl chlorides (**1**) with internal alkynes (**2**).[a]



1 **2** **3** **3'**

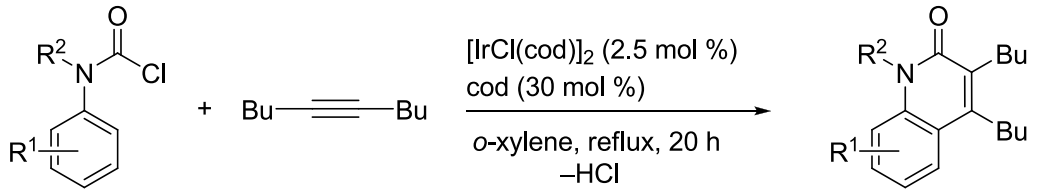
entry	**1**: R^1	**2**: R^2, R^3	**3**	% yield[b]	**3**/**3'**[c]
1	**1a**: H	**2a**: Bu, Bu	**3aa**	92 (82)[d]	–
2	**1a**: H	**2b**: $MeOCH_2$, $MeOCH_2$	**3ab**	62	–
3	**1a**: H	**2c**: Ph, Ph	**3ac**	67[e]	–
4	**1b**: MeO	**2c**: Ph, Ph	**3bc**	82[e]	–
5	**1b**: MeO	**2d**: 4-$MeOC_6H_4$, 4-$MeOC_6H_4$	**3bd**	89[e]	–
6	**1b**: MeO	**2e**: 4-ClC_6H_4, 4-ClC_6H_4	**3be**	76[e]	–
7	**1a**: H	**2f**: Me, Cy	**3af**	89	55/45
8	**1a**: H	**2g**: Ph, Me	**3ag**	95	58/42
9	**1a**: H	**2h**: $MeOCH_2$, *n*-C_5H_{11}	**3ah**	91	72/28
10	**1a**: H	**2i**: Me, 2-$MeOC_6H_4$	**3ai**	69	82/18

[a] Conditions: **1** (0.50 mmol), **2** (1.0 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), and cod (0.15 mmol, 30 mol %) in refluxing *o*-xylene (1.0 mL) for 20 h. [b] Isolated yields of **3** and **3'**. [c] The **3**/**3'** ratio was determined by GC. [d] In refluxing toluene. [e] $[IrCl(cod)]_2$ (0.025 mmol, 5.0 mol %), cod (0.50 mmol, 100 mol %).

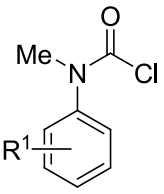
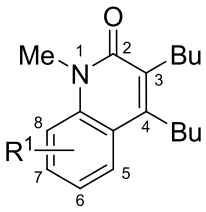
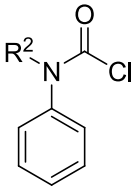
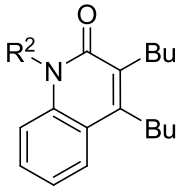
A wide variety of carbamoyl chlorides **1** can be easily synthesized from the corresponding amines.[12] Various carbamoyl chlorides (**1b**–**p**) thus obtained were reacted with **2a**, as shown in Table 4-3. Electron-rich (**1b**–**f**) and electron-poor (**1g**–**l**) phenyl moieties on the nitrogen smoothly participated in the cyclization to afford **3ba**–**fa** (entries 1–5) and **3ga**–**la** (entries 6–11) in good to excellent yields. Again, the cyclization of **1b** and **1e** was regioselective, affording **3ba** and **3ea**, respectively, as single isomers (entries 1 and 4). *N*-Phenylcarbamoyl chlorides bearing benzyl (**1m**), 4-methoxyphenylmethyl (**1n**), cyclohexyl (**1o**), and phenyl (**1p**) substituents on the nitrogen atom afforded the corresponding 2-quinolones (**3ma**–**pa**) in good to excellent yields (entries 12–15). The 4-methoxyphenylmethyl group of **3na** (entry 13) was removed by treatment with trifluoroacetic acid, affording 3,4-dibutyl-2-quinolone in 91% yield (Scheme 4-3).

Table 4-4 also shows a wide range of the substrate generality of **1** in the iridium-catalyzed system. Condensed ring systems (**3qa**–**ta**) were constructed using **1q**–**t** (entries 1–4). Besides 2-quinolones, *N*-butyl-*N*-2-thienylcarbamoyl chloride (**1u**) afforded the corresponding product **3ua** in excellent yield (entry 5). It is worth noting that the reaction could be applied not only to *N*-arylsubstituted carbamoyl chlorides but also to *N*-alkenyl-substituted **1v**, which provided the corresponding pyridone derivative **3va** in 52% yield (entry 6).

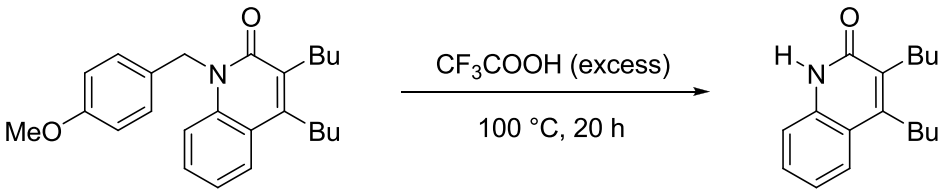
Table 4-3. Synthesis of **3** from **1** and **2a**.[a]



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

entry	**1**		**3**		% yield[b]
1		R^1 = 3-OMe **1b**		R^1 = 7-OMe **3ba**	85
2		R^1 = 4-OMe **1c**		R^1 = 6-OMe **3ca**	89
3		R^1 = 2-Me **1d**		R^1 = 8-Me **3da**	86
4		R^1 = 3-Me **1e**		R^1 = 7-Me **3ea**	93
5		R^1 = 4-Me **1f**		R^1 = 6-Me **3fa**	91
6		R^1 = 4-Cl **1g**		R^1 = 6-Cl **3ga**	87
7		R^1 = 4-Br **1h**		R^1 = 6-Br **3ha**	57[c]
8		R^1 = 4-CF_3 **1i**		R^1 = 6-CF_3 **3ia**	82[c]
9		R^1 = 4-CO_2Me **1j**		R^1 = 6-CO_2Me **3ja**	80
10		R^1 = 4-NO_2 **1k**		R^1 = 6-NO_2 **3ka**	73
11		R^1 = 4-CN **1l**		R^1 = 6-CN **3la**	59[c]
12		R^2 = $PhCH_2$ **1m**		**3ma**	88
13		R^2 = 4-$MeOC_6H_4CH_2$ **1n**		**3na**	66
14		R^2 = Cy **1o**		**3oa**	81
15		R^2 = Ph **1p**		**3pa**	88[c,d]

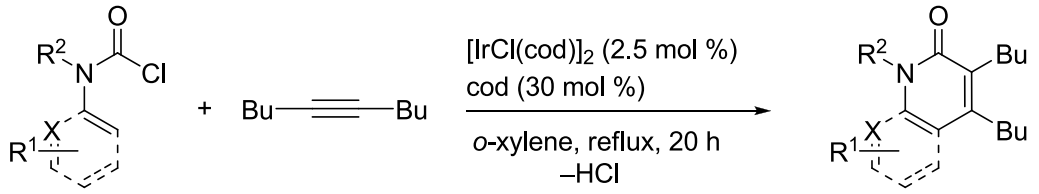
[a] Conditions: **1** (0.50 mmol), **2a** (1.0 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), and cod (0.15 mmol, 30 mol %) in refluxing *o*-xylene (1.0 mL) for 20 h. [b] Isolated yields. [c] $[IrCl(cod)]_2$ (0.025 mmol, 5.0 mol %). [d] For 36 h.



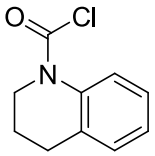
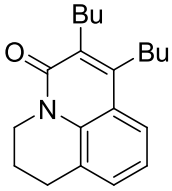
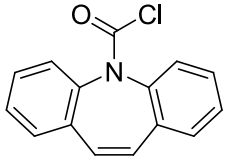
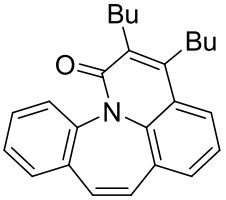
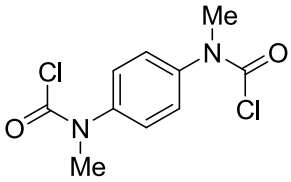
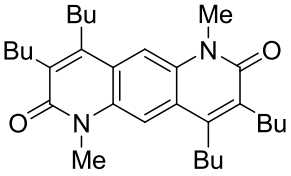
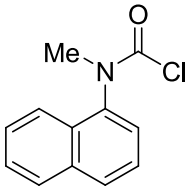
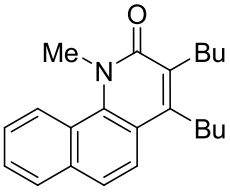
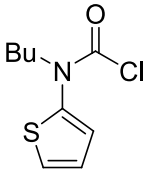
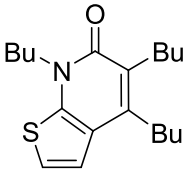
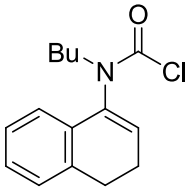
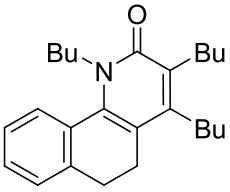
3na 91% yield

Scheme 4-3. Deprotection of the 4-methoxyphenylmethyl group on **3na**.

Table 4-4. Synthesis of **3** from **1** and **2a**.[a]

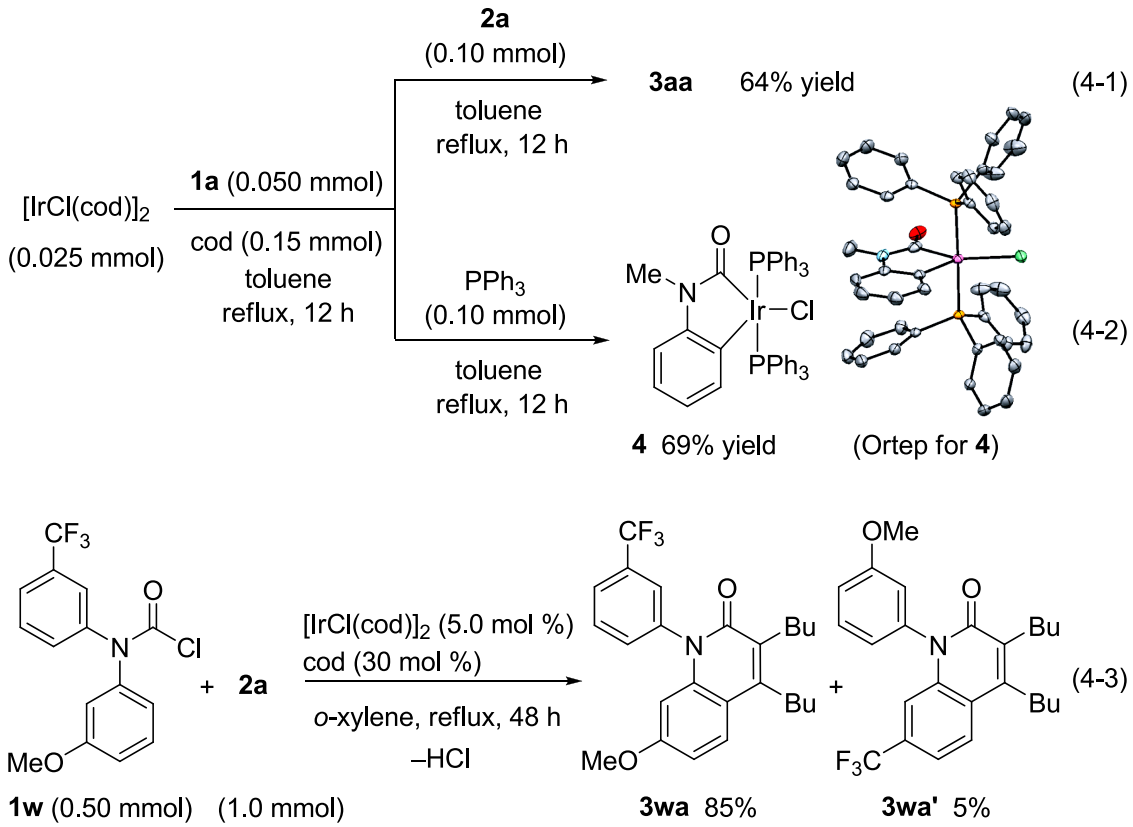


1 **2a** **3**

entry	**1**		**3**		% yield[b]
1		**1q**		**3qa**	51
2		**1r**		**3ra**	70
3		**1s**		**3sa**	68[c]
4		**1t**		**3ta**	90
5		**1u**		**3ua**	99
6		**1v**		**3va**	52[d,e]

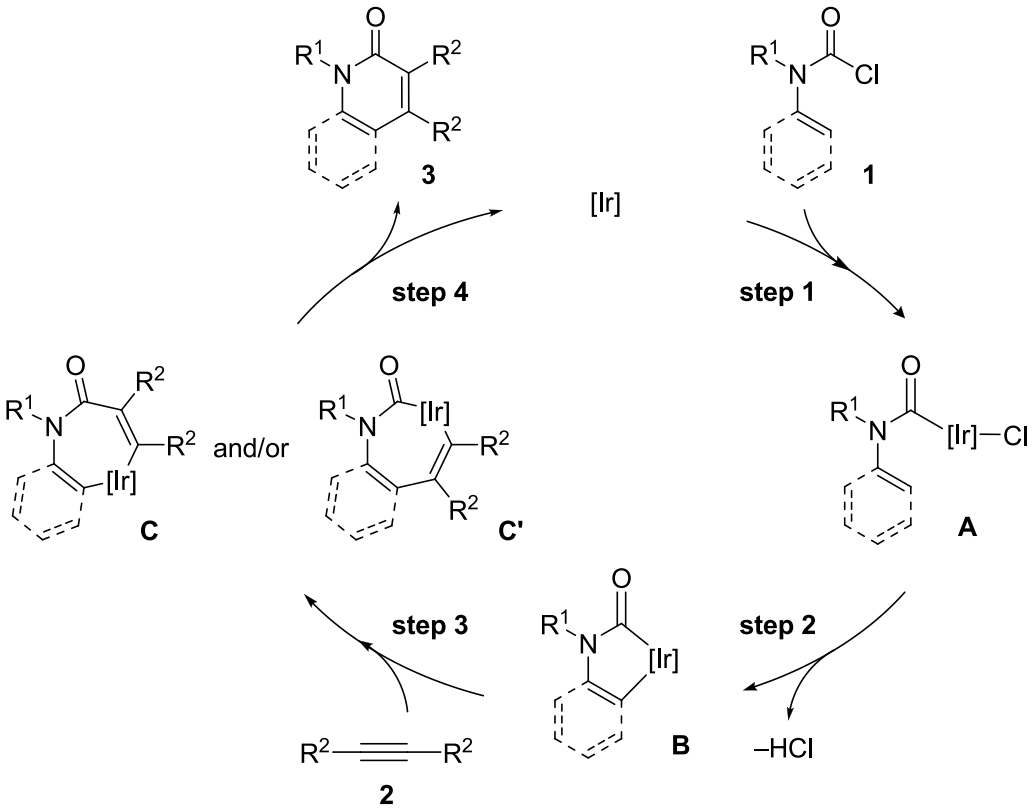
[a] Conditions: **1** (0.50 mmol), **2a** (1.0 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), and cod (0.15 mmol, 30 mol %) in refluxing *o*-xylene (1.0 mL) for 20 h. [b] Isolated yields. [c] **1s** (0.25 mmol). [d] $[IrCl(cod)]_2$ (0.025 mmol, 5.0 mol %). [e] For 48 h.

To gain further insight into the mechanism of the catalytic reaction, stoichiometric reactions between $[IrCl(cod)]_2$ and **1a** were carried out in the presence of added cod (eqs 4-1 and 4-2). After 12 h, **1a** was converted completely in refluxing toluene. When **2a** was then added to the reaction mixture under reflux, **3aa** was obtained in 64% yield (eq 4-1). In eq 4-1, however, no iridium complexes were identified. Therefore, instead of **2a**, PPh_3 (P/Ir = 2) was added into the reaction mixture (eq 4-2). As a result, iridium(III) metallacycle complex **4** was isolated in 69% yield, and the structure of **4** was confirmed by X-ray diffraction study. Iridacycle **4** did not provide **3aa** either catalytically or in a stoichiometric reaction with **2a** in refluxing toluene or xylene.[13] As for the cyclization, **1w** having both the 3-methoxyphenyl and 3-trifluoromethylphenyl moieties was reacted with **2a** (eq 4-3). The cyclization occurred preferentially at the more electron-rich phenyl ring (**3wa**/**3wa'** = 17/1).



A plausible reaction mechanism is shown in Scheme 4-4. Oxidative addition of **1** to the iridium(I) species (step 1) occurs, generating the carbamoyl-chloro-iridium(III) intermediate **A**.[14] Next, an intramolecular cyclization (step 2) affords a five-membered iridacycle **B**.[15] The relevant complex **4** was isolated with the aid of PPh_3 coordination in

eq 4-2. The cyclization must be electrophilic, since **3wa** was preferentially obtained over **3wa'** in eq 4-3. The construction of the iridacycle **B** would play a crucial role in suppressing the decarbonylation. Subsequent insertion of **2** (step 3) followed by reductive elimination (step 4) affords the 2-quinolone and regenerates the iridium(I) species.



Scheme 4-4. Plausible reaction mechanism.

4-3. Conclusion

In summary, 2-quinolones have been successfully obtained by the iridium-catalyzed annulation of *N*-arylcarbamoyl chlorides (**1**) with internal alkynes (**2**). Various substitutents and functional groups on substrates can be tollerated for the reaction system. It is likely that iridacycle **B** is a key intermediate in the catalytic reaction.

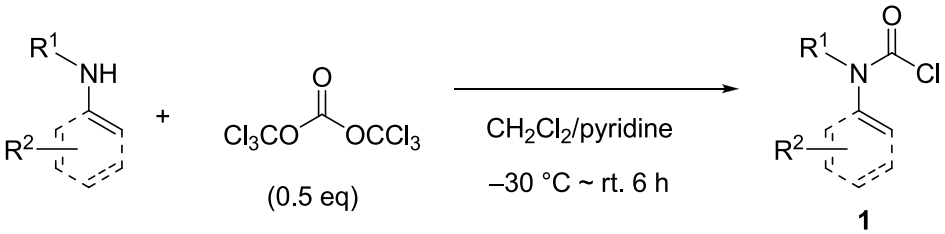
4-4. Experimental Section

Instrumentation and chemicals

All manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. All solvents were dried and purified by usual procedures.[16] Unless otherwise noted, materials obtained from

commercial suppliers were used without further purification. $[IrCl(cod)]_2$ was prepared according to the literature.[17] Carbamoyl chlorides **1a**, **1p** and **1r** were purchased from Aldrich and other carbamoyl chlorides were prepared from corresponding secondary amines or enamines according to the literatures.[12] Alkynes **2a**, **2c** and **2g** were purchased from TCI. Alkynes **2b**,[18] **2d**,[19] **2e**,[19] **2f**,[20] **2h**[21] and **2i**[22] were prepared according to the literatures. IR spectra were obtained on a SHIMADZU FTIR-8300 spectrometer. ^1H, ^{13}C and ^{31}P NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^1H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). The ^{31}P NMR chemical shifts are reported relative to 85% H_3PO_4 (0.00 ppm) as an external standard. EI-MS were recorded on a Shimadzu GCMS-QP5050A with a direct inlet. MALDI-TOF-MS spectra were recorded on a Bruker Autoflex. High-resolution mass spectra (EI-HRMS) were obtained with a JEOL SX-102A spectrometer. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using a Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). Melting points were measured on a Yanako MP-J3 apparatus. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$.

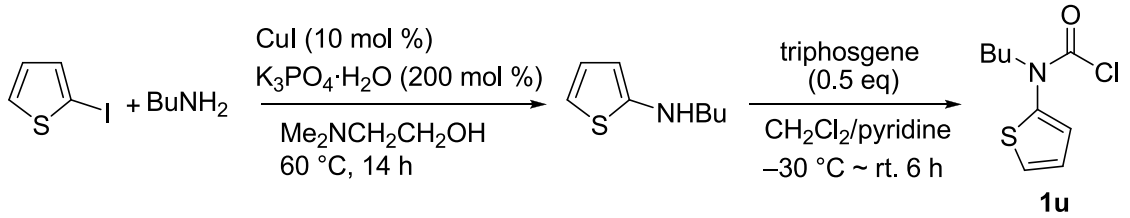
General procedures for synthesis of carbamoyl chlorides (1a–t)[12]



A 100 mL two-necked flask with a magnetic stir bar was evacuated and backfilled with argon three times. Triphosgene (5.0 mmol) and CH_2Cl_2 (30 mL) were added to the flask. The mixture was cooled at –30 °C and dry pyridine (3.0 mL) was slowly added to the flask (*Caution: highly toxic phosgene was generated*). After stirring for 15 min at –30 °C, secondary amine or enamine (10 mmol) was slowly added to the mixture. The mixture was warmed to room temperature and stirred for 6 h at room temperature. The reaction mixture was carefully quenched by 1N HCl (10 mL) and was extracted with CH_2Cl_2 (5 mL x 3). The organic layer was washed with water and brine, then dried over $MgSO_4$. After the filtration, the solution was concentrated to dryness. The crude product

was purified by silica gel column chromatography. Further purification was carried out by recrystallization or distillation under vacuum.

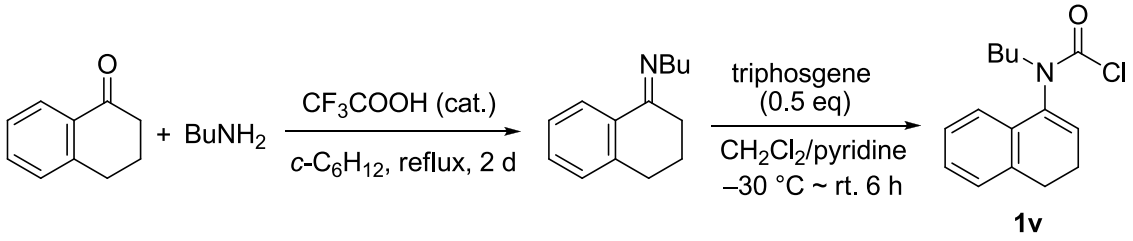
Procedure for synthesis of 1u



1u

N-Butyl-2-thiophenanime[23] was prepared according to the literature. Because the amine was sensitive to air, the carbamoylation with triphosgene was carried out immediately.

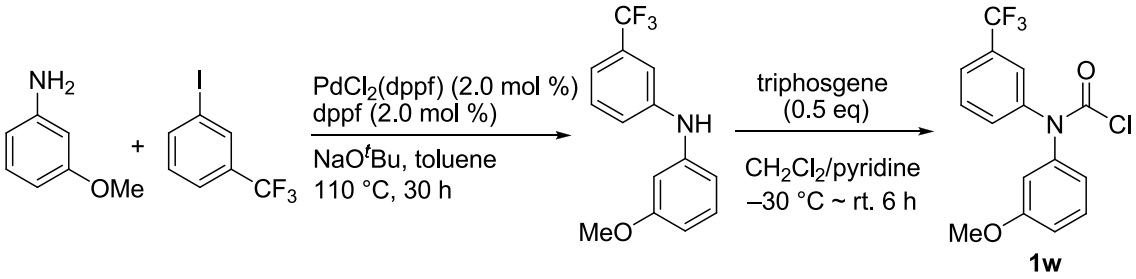
Procedure for synthesis of 1v



1v

N-(3,4-dihydro-1(2*H*)-naphthalenylidene)-1-butanamine[24] was prepared according to the literature and subjected to the carbamoylation.

Procedure for synthesis of 1w



1w

N-(3-Methoxyphenyl)-3-(trifluoromethyl)aniline[25] was prepared as follows. $PdCl_2$(dppf) (163 mg, 0.20 mmol) and dppf (111 mg, 0.20 mmol) were added to a 100 mL two-necked flask with a magnetic stir bar and the flask was evacuated and backfilled with argon three times. Then toluene (30 mL), KO^{t}Bu (2.0 g, 20.8 mmol), *m*-anisidine (10 mmol) and 3-trifluoromethyliodobenzene (17 mmol) were added to the flask and the mixture was stirred at 110 °C for 30 h. After cooling to room temperature,

H_2O (30 mL) was added to the flask and the mixture was extracted with EtOAc. The organic layer was washed with water and brine, then dried over $MgSO_4$. After the filtration, the solution was concentrated to dryness. The crude product was purified by silica gel column chromatography using hexane-EtOAc (9:1) as an eluent. *N*-(3-Methoxyphenyl)-3-(trifluoromethyl)aniline was obtained in 86% yield (2.3 g) as a colorless oil. The carbamoylation was carried out to give **1w**.

General procedures in Table 4-1

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and additives (0–0.50 mmol) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. **1a** (84.8 mg, 0.50 mmol) and **2a** (180 μL, 1.0 mmol) were added to the flask and the mixture was heated under reflux (bath temp. 120 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and added tridecane (50 μL, 0.205 mmol) as an internal standard. The yield of the products **3aa** was determined by GC analysis.

General procedures for synthesis of 2-quinolones (3) (Tables 4-2, 4-3 and 4-4)

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) and 1,5-cyclooctadiene (18 μL, 0.15 mmol) were added to the flask. A carbamoyl chloride (**1**) (0.50 mmol) and an alkyne (**2**) (1.0 mmol) were added to the flask and the mixture was stirred under reflux (bath temp. 155 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product was isolated by silica gel column chromatography.

Procedure for synthesis of 3,4-dibutyl-2(1*H*)-quinolone from 3na[26] (Scheme 4-3)

3na (56.6 mg, 0.15 mmol) and trifluoroacetic acid (1.0 mL) were added to a 5 mL screw vial with a magnetic stir bar. The vial was capped and the mixture was stirred at 100 °C for 20 h. After cooling to room temperature, the mixture was evaporated and the desired product was isolated in 91% yield by silica gel column chromatography using hexane-EtOAc (1:1) as an eluent.

Procedures in eqs 4-1 and 4-2

$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL) and 1,5-cyclooctadiene (18 μL, 0.15 mmol) were added to the flask. **1a** (8.4 mg, 0.050 mmol) and tridecane (12 μL, 0.050 mmol) as an internal standard were added to the flask and the mixture was stirred under reflux (bath temp. 120 °C) for 12 h under an argon atmosphere. A small aliquot (0.01 mL) was taken out from the reaction mixture and the samples were diluted with diethyl ether (0.02 mL) and analyzed by GC. Subsequently, to the reaction mixture **2a** (18 μL, 0.10 mmol) was added and the mixture was stirred under reflux (bath temp. 120 °C) for 12 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (2.0 ml) and the yield of **3aa** was determined by GC analysis.

Instead of **2a**, PPh_3 (26.2 mg, 0.10 mmol) was added to the flask and the mixture was stirred under reflux (bath temp. 120 °C) for 12 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the crude product was washed with diethyl ether (1 mL x 3) to give yellow solids of **4** (30.5 mg, 69% yield) with a small amount of undefined impurities. Further purification was done by recrystallization from CH_2Cl_2/hexane solution. The iridacycle **4** is stable under air and does not react with **2a** in refluxing toluene (bath temp. 120 °C).

Alternative procedure for synthesis of 4

$[IrCl(cod)]_2$ (33.6 mg, 0.050 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then toluene (1.0 mL), 1,5-cyclooctadiene (18 μL, 0.15 mmol), $NaHCO_3$ (10.1 mg, 0.12 mmol) and **1a** (20.4 mg, 0.12 mmol) were added to the flask. The mixture was stirred under reflux (bath temp. 120 °C) for 12 h under an argon atmosphere. Subsequently, PPh_3 (62.9 mg, 0.24 mmol) was added to the solution and the mixture was stirred under reflux (bath temp. 120 °C) for further 12 h. After cooling to room temperature, the reaction mixture was diluted with $CHCl_3$ (5.0 ml) and filtrated to remove insoluble solids. The filtrate was evaporated and the crude product was washed with diethyl ether (2 mL x 3) to give yellow solids of **4** (72.4 mg, 82% yield).

Procedure in eq 4-3

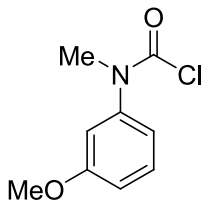
$[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) was added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) and 1,5-cyclooctadiene (18 μL, 0.15 mmol) were

added to the flask. Substrates **1w** (0.50 mmol) and **2a** (1.0 mmol) were added to the flask and the mixture was stirred under reflux (bath temp. 155 °C) for 48 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product was isolated by silica gel column chromatography using toluene–EtOAc (50:1) as an eluent.

Characterization of the Compounds

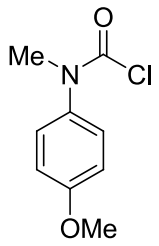
Carbamoyl Chlorides

N-(3-Methoxyphenyl)-*N*-methylcarbamoyl chloride (**1b**)



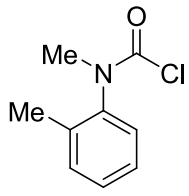
White solids: m.p. 72-73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (t, J = 8.2 Hz, 1H), 6.88 (d, J = 8.2 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 6.78 (s, 1H), 3.78 (s, 3H), 3.33 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.1, 148.7, 143.9, 130.0, 119.3, 113.8, 113.1, 55.2, 40.1. IR (KBr): 1733.9, 1215.1, 704.0 cm^{-1}. EI-MS: *m/z* 201 (16%, $[M+2]^+$), 200 (4, $[M+1]^+$), 199 (51, $[M]^+$), 164 (100), 136 (44). Anal. Calcd. for $C_9H_{10}ClNO_2$: C, 54.15; H, 5.05. Found: C, 54.01; H, 4.96.

N-(4-Methoxyphenyl)-*N*-methylcarbamoyl chloride (**1c**)[27]



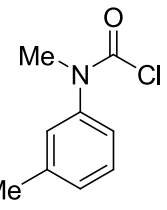
Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J = 9.1 Hz, 2H), 6.82 (t, J = 9.1 Hz, 2H), 3.72 (s, 3H), 3.24 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.2, 149.3, 136.0, 128.3, 114.5, 55.3, 40.3. IR (neat): 1735.8, 1514.0, 1249.8, 1035.7 cm^{-1}. EI-MS: *m/z* 201 (26%, $[M+2]^+$), 200 (5, $[M+1]^+$), 199 (88, $[M]^+$), 164 (54), 136 (100).

N-Methyl-*N*-(*o*-tolyl)carbamoyl chloride (**1d**)



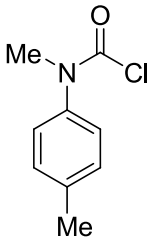
White solids: m.p. 57-58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (t, J = 7.7 Hz, 1H), 7.17-7.19 (m, 1H), 7.02-7.07 (m, 2H), 3.35 (s, 3H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.9, 143.0, 139.5, 129.2, 129.1, 127.7, 124.2, 40.2, 21.1. IR (KBr): 1733.9, 1255.6, 856.3 cm^{-1}. EI-MS: *m/z* 185 (10%, $[M+2]^+$), 184 (2, $[M+1]^+$), 183 (29, $[M]^+$), 148 (93), 120 (74), 91 (100). Anal. Calcd. for $C_9H_{10}ClNO$: C, 58.86; H, 5.49. Found: C, 58.80; H, 5.42.

N-Methyl-*N*-(*m*-tolyl)carbamoyl chloride (**1e**)



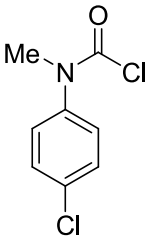
White solids: m.p. 49-50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 7.7 Hz, 1H), 7.16-7.18 (m, 1H), 7.01-7.05 (m, 2H), 3.34 (s, 3H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.0, 143.0, 139.6, 129.2, 129.1, 127.8, 124.2, 40.2, 21.1. IR (KBr): 1728.1, 1269.1, 705.9 cm^{-1}. EI-MS: *m/z* 185 (14%, $[M+2]^+$), 184 (3, $[M+1]^+$), 183 (47, $[M]^+$), 148 (100), 120 (50), 91 (79). Anal. Calcd. for $C_9H_{10}ClNO$: C, 58.86; H, 5.49. Found: C, 58.80; H, 5.38.

N-Methyl-*N*-(*p*-tolyl)carbamoyl chloride (**1f**)



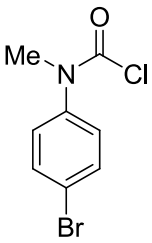
White solids: m.p. 64-65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.2 Hz, 2H), 3.34 (s, 3H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.2, 140.7, 138.5, 130.1, 127.0, 40.3, 21.1. IR (KBr): 1733.9, 1508.2, 1271.0, 860.2 cm^{-1}. EI-MS: *m/z* 185 (19%, $[M+2]^+$), 184 (3, $[M+1]^+$), 185 (57, $[M]^+$), 148 (100), 120 (72), 91 (96). Anal. Calcd. for $C_9H_{10}ClNO$: C, 58.86; H, 5.49. Found: C, 58.60; H, 5.38.

N-(4-Chlorophenyl)-*N*-methylcarbamoyl chloride (**1g**)[27]



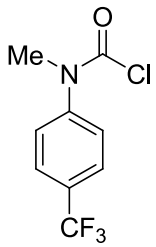
White solids: m.p. 64-65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 3.34 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.8, 141.5, 134.3, 129.7, 128.7, 40.2. IR (KBr): 1743.5, 1488.9, 1257.5, 840.9 cm^{-1}. EI-MS: *m/z* 207 (2%, $[M+4]^+$), 205 (15, $[M+2]^+$), 203 (27, $[M]^+$), 168 (100), 140 (60).

N-(4-Bromophenyl)-*N*-methylcarbamoyl chloride (**1h**)



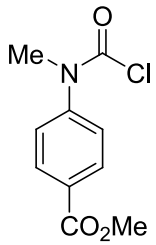
White solids: m.p. 64-65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.6 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 3.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.49, 141.9, 132.6, 129.0, 127.1, 40.1. IR (KBr): 1741.6, 1485.1, 1257.5, 717.5 cm^{-1}. EI-MS: *m/z* 251 (17%, $[M+4]^+$), 249 (56, $[M+2]^+$), 247 (47, $[M]^+$), 212 (100), 192 (93). Anal. Calcd. for C_8H_7BrNO: C, 38.67; H, 2.84. Found: C, 38.63; H, 2.75.

N-Methyl-*N*-(4-trifluoromethylphenyl)carbamoyl chloride (**1i**)



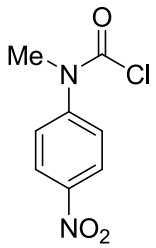
White solids: m.p. 57-58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 3.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.6, 145.9, 130.5, 127.9, 126.7 (q, $^3J_{C\text{-}F}$ = 3.0 Hz), 123.6 (q, $^1J_{C\text{-}F}$ = 272 Hz), 40.3. IR (KBr): 1735.8, 1325.0, 1109.0, 850.5 cm^{-1}. EI-MS: *m/z* 239 (4%, $[M+2]^+$), 238 (2, $[M+1]^+$), 237 (22, $[M]^+$), 202 (100), 174 (56). EI-HRMS: Calcd. for $C_9H_7ClF_3NO$ ($[M]^+$), 237.0168. Found, 237.0175.

4-[(Chlorocarbonyl)methylamino]benzoic acid methyl ester (**1j**)



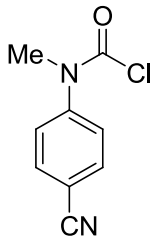
White solids: m.p. 58-59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 3.84 (s, 3H), 3.34 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.7, 148.4, 146.6, 130.7, 129.7, 127.2, 52.1, 40.2. IR (KBr): 1724.2, 1735.8, 1604.7, 1288.4, 1116.7, 704.0 cm^{-1}. EI-MS: *m/z* 229 (13%, $[M+2]^+$), 228 (4, $[M+1]^+$), 227 (38, $[M]^+$), 192 (100), 165 (52). Anal. Calcd. for $C_{10}H_{10}ClNO_3$: C, 52.76; H, 4.43. Found: C, 52.69; H, 4.31.

N-Methyl-*N*-(4-nitrophenyl)carbamoyl chloride (**1k**)[27]



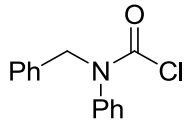
White solids: m.p. 99-100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28-8.33 (m, 2H). 7.50-7.55 (m, 2H), 3.50 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.0, 146.6, 127.7 (br), 124.8, 40.4. IR (KBr): 1733.9, 1344.3, 1253.6, 866.0 cm^{-1}. EI-MS: *m/z* 216 (4%, $[M+2]^+$), 215 (2, $[M+1]^+$), 214 (22, $[M]^+$), 179 (100), 105 (38).

N-(4-Cyanophenyl)-*N*-methylcarbamoyl chloride (**1l**)



White solids: m.p. 75-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 3.46 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.7, 146.4, 133.4, 127.9, 117.7, 111.9, 40.4. IR (KBr): 2231.5, 1739.7, 1508.2, 1257.5, 858.3 cm^{-1}. EI-MS: *m/z* 196 (4%, $[M+2]^+$), 195 (2, $[M+1]^+$), 194 (23, $[M]^+$), 159 (100), 131 (39). Anal. Calcd. for $C_9H_7ClN_2O$: C, 55.54; H, 3.63. Found: C, 55.50; H, 3.49.

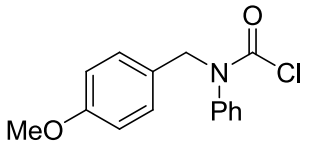
N-Benzyl-*N*-phenylcarbamoyl chloride (**1m**)



White solids: m.p. 45-46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.34 (m, 6H), 7.19 (br, 2H), 7.00 (br, 2H), 4.85 (s, 2H). $^{13}C\{^1H\}$

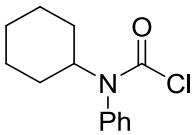
NMR (100 MHz, $CDCl_3$): δ 149.5, 141.4, 135.4, 129.2, 128.8, 128.5, 128.3, 128.0, 56.4. IR (KBr): 1732.0, 1247.9, 698.2 cm^{-1}. EI-MS: *m/z* 247 (8%, $[M+2]^+$), 248 (4, $[M+1]^+$), 247 (32, $[M]^+$), 119 (100), 91(80). Anal. Calcd. for $C_{14}H_{12}ClNO$: C, 68.44; H, 4.92. Found: C, 68.47; H, 509.

N-(4-Methoxyphenylmethyl)-*N*-phenylcarbamoyl chloride (**1n**)



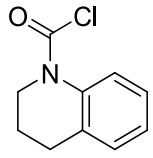
White solids: m.p. 56-57 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.31-7.34 (m, 3H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.99 (br, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.79 (s, 2H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.4, 149.5, 141.5, 130.4, 129.3, 128.5, 127.6, 113.9, 56.0, 55.2. IR (KBr): 1720.4, 1514.0, 1236.3, 603.7 cm^{-1}. EI-MS: *m/z* 277 (1%, $[M+2]^+$), 275 (3, $[M]^+$), 210 (4), 156 (100). Anal. Calcd. for $C_{15}H_{14}ClNO_2$: C, 65.34; H, 5.12. Found: C, 65.40; H, 5.09.

N-Cyclohexyl-*N*-phenylcarbamoyl chloride (**1o**)



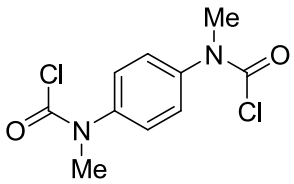
White solids: m.p. 70-71 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26-7.42 (m, 3H), 7.08-7.12 (m, 2H), 4.21-5.01 (m, 1H), 1.92 (d, *J* = 10.9 Hz, 2H), 1.73 (d, *J* = 14.0 Hz, 2H), 1.54 (d, *J* = 13.1 Hz, 1H), 1.26-1.39 (m, 2H), 1.06-1.18 (m, 2H), 0.83-0.96 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.9, 138.6, 130.0, 128.9, 128.7, 59.9, 31.3, 25.5, 24.9. IR (KBr): 2931.6, 1741.6, 1220.9, 704.0 cm^{-1}. EI-MS: *m/z* 239 (1%, $[M+2]^+$), 237 (3, $[M+1]^+$), 237 (22, $[M]^+$), 202 (29), 155 (70), 119 (92), 55 (100). Anal. Calcd. for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.78. Found: C, 65.67; H, 6.84.

3,4-Dihydro-1(2*H*)-quinolinecarbonyl chloride (**1q**)[28]



Colorless oil: ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (br, 1H), 7.11-7.24 (m, 3H), 3.94 (t, *J* = 6.3 Hz, 2H), 2.81 (t, *J* = 6.3 Hz, 2H), 2.00-2.07 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.5, 137.5, 131.6, 128.5, 126.1, 125.7, 124.5, 48.6, 26.5, 23.6. IR (neat): 2948.9, 1733.9, 1490.9, 759.9 cm^{-1}. EI-MS: *m/z* 197 (10%, $[M+2]^+$), 196 (3, $[M+1]^+$), 195 (29, $[M]^+$), 132 (100).

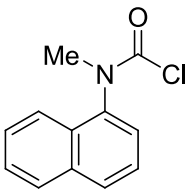
N,N'-Dimethyl-*N,N'*-*p*-phenylenedicarbamoyl chloride (**1s**)[29]



White solids: m.p. 158-159 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 (s, 4H), 3.41 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.9, 142.9, 128.7, 40.3. IR (KBr): 1735.8, 1512.1, 1352.0, 1244.0, 833.2 cm^{-1}. EI-MS: *m/z* 264 (4%,

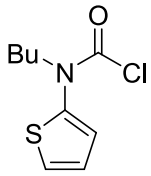
[M+4]$^+$), 263 (3, [M+3]$^+$), 262 (29, [M+2]$^+$), 260 (49, [M]$^+$), 225 (72), 140 (100).

N-Methyl-*N*-(1-naphthyl)carbamoyl chloride (**1t**)[30]



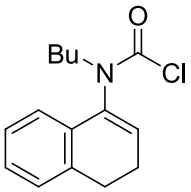
White solids: m.p. 91-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (t, J = 9.1 Hz, 2H), 7.80 (d, J = 8.6 Hz, 1H), 7.46-7.62 (m, 3H), 7.39 (dd, J = 7.2, 0.9 Hz, 1H), 3.44 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.0, 139.3, 134.5, 129.5, 129.2, 128.6, 127.6, 126.7, 125.65, 125.59, 121.8, 40.0. IR (KBr): 1728.1, 1271.0, 775.3 cm^{-1}. EI-MS: *m/z* 211 (7%, [M+2]$^+$), 210 (3, [M+1]$^+$), 219 (39, [M]$^+$), 184 (31), 162 (100).

N-Butyl-*N*-(2-thienyl)carbamoyl chloride (**1u**)



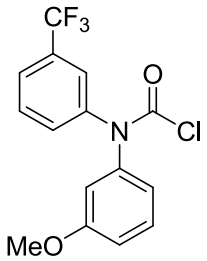
Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, J = 5.0 Hz, 1H), 6.91-6.95 (m, 1H), 6.89 (m, 1H), 3.71 (t, J = 7.2 Hz, 2H), 1.57-1.64 (m, 2H), 1.28-1.39 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.6, 143.3, 126.3, 125.5, 125.2, 53.6, 29.3, 19.4, 13.5. IR (neat): 2960.5, 1739.7, 1213.1, 702.0 cm^{-1}. EI-MS: *m/z* 219 (14%, [M+2]$^+$), 218 (3, [M+1]$^+$), 217 (45, [M]$^+$), 182 (15), 125 (74), 41 (100). Anal. Calcd. for $C_9H_{12}ClNOS$: C, 49.65; H, 5.56. Found: C, 49.80; H, 5.57.

N-Butyl-*N*-(3,4-dihydro-1-naphthalenyl)carbamoyl chloride (**1v**)



Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14-7.21 (m, 3H), 7.03-7.07 (m, 1H), 6.01 (t, J = 4.5 Hz, 1H), 3.87-3.94 (m, 1H), 3.10-3.17 (m, 1H), 2.83 (t, J = 8.2 Hz, 2H), 2.42-2.49 (m, 2H), 1.53-1.72 (m, 2H), 1.25-1.39 (m, 2H), 0.91 (t, J = 7.7 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.4, 138.0, 136.3, 130.5, 129.1, 128.0, 127.8, 126.5, 121.6, 50.5, 29.7, 26.8, 22.7, 19.6, 13.5. IR (neat): 2935.5, 1737.7, 1240.1, 767.6 cm^{-1}. EI-MS: *m/z* 265 (18%, [M+2]$^+$), 264 (12, [M+1]$^+$), 263 (48, [M]$^+$), 228 (24), 200 (100), 129 (97). EI-HRMS: Calcd. for $C_{15}H_{18}ClNO$ ([M]$^+$), 236.1077. Found, 263.1077.

N-(3-Methoxyphenyl)-*N*-[(3-trifluoromethylphenyl)]carbamoyl chloride (**1w**)

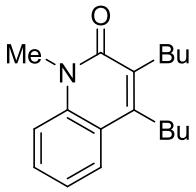


White solids: m.p. 83-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.46-7.56 (m, 3H), 7.28-7.34 (m, 1H), 6.88-6.93 (m, 3H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.4, 148.9, 142.5, 131.7 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 130.3, 130.0, 129.0 (br), 124.1 (br), 123.3 (q, $^1J_{C\text{-}F}$ = 273 Hz), 120.6 (br), 114.0 (br), 55.4. IR (KBr): 1733.9,

1330.8, 1122.5, 752.2 cm^{-1}. EI-MS: *m/z* 331 (20%, $[M+2]^+$), 330 (12, $[M+1]^+$), 329 (59, $[M]^+$), 294 (100), 266 (41). Anal. Calcd. for $C_{15}H_{11}ClF_3NO_2$: C, 54.64; H, 3.36. Found: C, 54.72; H, 3.22.

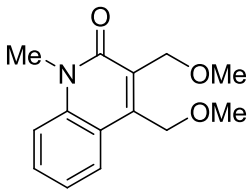
2-Quinolones

3,4-Dibutyl-1-methyl-2(*1H*)-quinolinone (**3aa**)



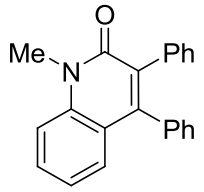
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). Colorless oil, 125 mg, 92% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.2 Hz, 1 H), 7.47 (t, J = 8.6 Hz, 1H), 7.33 (d, J = 8.6 Hz, 1 H), 7.22 (t, J = 8.2 Hz, 1H), 3.72 (s, 3H), 2.86 (t, J = 7.2 Hz, 2H), 2.72 (t, J = 7.2 Hz, 2H), 1.40-1.62 (m, 8H), 0.99 (t, J = 7.2 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.1, 145.0, 138.7, 131.3, 129.0, 124.9, 121.7, 120.6, 114.2, 32.0, 31.4, 29.7, 28.4, 27.7, 23.19, 23.16, 13.9, 13.8. IR (neat): 2956.7, 1635.5, 750.3 cm^{-1}. EI-MS: *m/z* 272 (4%, $[M+1]^+$), 271 (18, $[M]^+$), 270 (8, $[M-1]^+$), 242 (48), 214 (83), 187 (100). Anal. Calcd. for $C_{18}H_{25}NO$: C, 79.66; H, 9.28. Found: C, 79.50; H, 9.43.

3,4-Bis(methoxymethyl)-1-methyl-2(*1H*)-quinolinone (**3ab**)



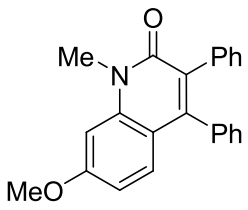
Isolated by column chromatography (silica gel, hexane/AcOEt = 1/1). Pale yellow solids, 77.0 mg, 62% yield: m.p. 69-70 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 7.7 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.34 (d, J = 8.6 Hz, 1H), 7.26 (t, J = 7.7 Hz, 1H), 4.82 (s, 2H), 4.70 (s, 2H), 3.74 (s, 3H), 3.45 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.8, 143.9, 139.5, 130.5, 128.5, 126.5, 122.1, 119.9, 114.1, 67.4, 65.6, 58.41, 58.40, 30.0. IR (KBr): 2925.8, 1637.5, 1091.6, 756.0 cm^{-1}. EI-MS: *m/z* 248 (3%, $[M+1]^+$), 247 (23, $[M]^+$), 232 (100), 217 (24), 200 (48), 172 (55), 144 (51). Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93. Found: C, 67.70; H, 6.85.

1-Methyl-3,4-diphenyl-2(*1H*)-quinolinone (**3ac**)[31]



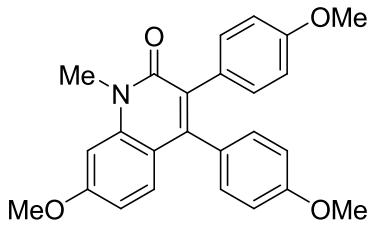
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 105 mg, 67% yield: m.p. 216-217 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, J = 7.3 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.22-7.35 (m, 4H), 7.08-7.20 (m, 8H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.6, 147.5, 139.4, 136.2, 135.8, 131.9, 130.5, 130.2, 129.7, 128.3, 127.8, 127.4, 127.3, 126.7, 121.7, 121.3, 113.9, 29.9. IR (KBr): 1633.6, 1587.3, 1311.5, 700.1 cm^{-1}. EI-MS: *m/z* 311 (50%, $[M+1]^+$), 310 (100, $[M]^+$), 294 (10), 267 (8).

7-Methoxy-1-methyl-3,4-diphenyl-2(*1H*)-quinolinone (**3bc**)



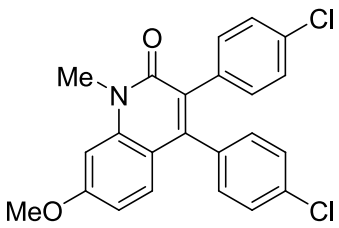
Isolated by column chromatography (silica gel, hexane/AcOEt = 1/1). White solids, 140 mg, 82% yield: m.p. 178-179 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16-7.25 (m, 4H), 7.04-7.15 (m, 7H), 6.85 (d, J = 2.3 Hz, 1H), 6.68 (dd, J = 9.1, 2.3 Hz, 1H), 3.87 (s, 3H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.9, 161.3, 147.5, 140.9, 136.4, 136.0, 130.6, 129.7, 129.6, 128.8, 127.7, 127.3, 127.2, 126.4, 115.3, 109.0, 98.4, 55.4, 29.9. IR (KBr): 1635.5, 1614.3, 1317.3, 698.2 cm^{-1}. EI-MS: *m/z* 342 (14%, $[M+1]^+$), 341 (50, $[M]^+$), 340 ($[M-1]^+$, 100), 325 (5), 134 (11). EI-HRMS: Calcd. for $C_{23}H_{19}NO_2$ ($[M]^+$), 341.1416. Found, 341.1408.

7-Methoxy-3,4-bis(4-methoxyphenyl)-1-methyl-2(*1H)*-quinolinone (**3bd**)



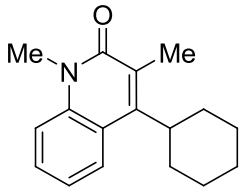
Isolated by column chromatography (silica gel, CH_2Cl_2/AcOEt = 10/1). White solids, 179 mg, 89% yield: m.p. 176-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 2.3 Hz, 1H), 7.03 (t, J = 8.6 Hz, 4H), 6.86 (d, J = 1.8 Hz, 1H), 6.81 (d, J = 8.6 Hz, 2H), 6.70-6.75 (m, 3H), 3.90 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 161.1, 158.5, 157.9, 147.0, 140.8, 131.8, 131.0, 129.7, 128.8, 128.55, 128.47, 115.7, 113.3, 112.8, 108.9, 98.3, 55.4, 54.95, 54.88, 29.9. IR (KBr): 1608.5, 1247.9, 1033.8, 825.5 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 402 (63%, $[M+1]^+$), 401 (100, $[M]^+$). Anal. Calcd. for $C_{25}H_{23}NO_4$: C, 74.79; H, 5.77. Found: C, 74.63; H, 5.64.

3,4-Bis(4-chlorophenyl)-7-methoxy-1-methyl-2(*1H*)-quinolinone (**3be**)



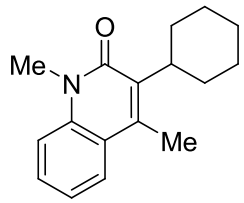
Isolated by column chromatography (silica gel, CH_2Cl_2/AcOEt = 15/1). White solids, 153 mg, 76% yield: m.p. 197-198 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 8.6 Hz, 2H), 7.12-7.18 (m, 3H), 7.00-7.04 (m, 4H), 6.86 (d, J = 2.3 Hz, 1H), 6.72 (dd, J = 9.1, 2.3 Hz, 1H), 3.91 (s, 3H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.7, 161.6, 146.6, 141.1, 134.7, 134.3, 133.7, 132.7, 132.1, 131.0, 129.6, 128.4, 127.79, 127.75, 114.9, 109.4, 98.6, 55.5, 30.1. IR (KBr): 1631.7, 1610.5, 1091.6, 825.5 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 414 (24%, $[M+4]^+$), 413 (24, $[M+3]^+$), 412 (71%, $[M+2]^+$), 410 (100, $[M]^+$). Anal. Calcd. for $C_{23}H_{17}Cl_2NO_2$: C, 67.33; H, 4.18. Found: C, 67.07; H, 4.08.

4-Cyclohexyl-1,3-dimethyl-2(*1H*)-quinolinone (**3af**)



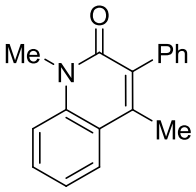
Isolated by column chromatography (silica gel, hexane/AcOEt = 7/1). White solids, 62.9 mg, 49% yield: m.p. 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 50 ºC): δ 8.05 (brs, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 6.8 Hz, 1H), 3.73 (s, 3H), 3.30 (m, 1H), 2.36 (s, 3H), 2.05-2.20 (m, 2H), 1.61-1.98 (m, 5H), 1.35-1.52 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 50 ºC): δ 162.9, 148.6, 138.9, 128.7, 127.2, 125.6, 121.1, 120.7, 114.4, 41.50, 30.26, 30.06, 37.4, 26.2, 14.5. IR (KBr): 2923.9, 1629.7, 1589.2, 763.8 cm^{-1}. EI-MS: *m/z* 256 (6%, $[M+1]^+$), 255 (46, $[M]^+$), 254 (100), 212 (24), 200 (28). Anal. Calcd. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29. Found: C, 79.66; H, 8.23.

3-Cyclohexyl-1,4-dimethyl-2(*1H*)-quinolinone (**3af'**)



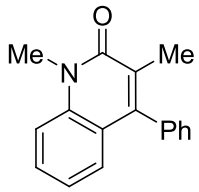
Isolated by column chromatography (silica gel, hexane/AcOEt = 10/1). White solids, 51.5 mg, 40% yield: m.p. 125-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.21 (t, J = 7.7 Hz, 1H), 3.69 (s, 3H), 3.11 (brs, 1H), 2.51 (s, 3H), 2.31 (brs, 2H), 1.85 (brs, 2H), 1.73 (brs, 1H), 1.56 (d, J = 11.8 Hz, 2H), 1.37 (brs, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.5, 140.4, 138.5, 135.0, 129.0, 125.1, 121.8, 121.5, 113.8, 40.4, 29.39, 29.30, 27.2, 26.0, 15.2. IR (KBr): 2923.9, 1624.4, 1589.2, 746.4 cm^{-1}. EI-MS: *m/z* 256 (10%, $[M+1]^+$), 255 (51, $[M]^+$), 240 (66), 212 (64), 200 (73), 187 (100). EI-HRMS: Calcd. for $C_{17}H_{21}NO$ ($[M]^+$), 255.1623. Found, 255.1624.

1,4-Dimethyl-3-phenyl-2(*1H*)-quinolinone (**3ag**)



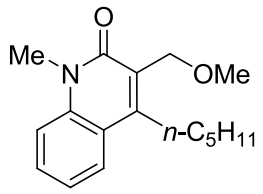
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 69.1 mg, 55% yield: m.p. 136-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 6.8 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 7.33-7.45 (m, 4H), 7.25-7.29 (m, 3H), 3.75 (s, 3H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 142.2, 139.0, 136.7, 132.3, 130.01, 129.95, 128.1, 127.3, 125.5, 121.9, 121.4, 114.1, 29.7, 16.8. IR (KBr): 1629.7, 1591.2, 752.2, 698.2 cm^{-1}. EI-MS: *m/z* 250 (11%, $[M+1]^+$), 249 (54, $[M]^+$), 248 (100, $[M-1]^+$). EI-HRMS: Calcd. for $C_{17}H_{15}NO$ ($[M]^+$), 249.1154. Found, 294.1153.

1,3-Dimethyl-4-phenyl-2(*1H*)-quinolinone (**3ag'**)[32]



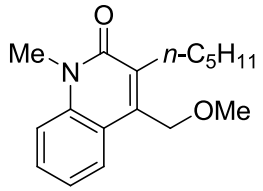
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 49.7 mg, 40% yield: m.p. 123-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.53 (m, 4H), 7.39 (d, J = 8.6 Hz, 1H), 7.22 (d, J = 6.8 Hz, 2H), 7.05-7.13 (m, 2H), 3.82 (s, 3H), 2.03 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.6, 146.6, 138.5, 137.0, 129.2, 128.8, 128.6, 127.8, 127.6, 121.66, 121.58, 113.8, 29.9, 15.2. IR (KBr): 1637.5, 754.1 cm^{-1}. EI-MS: *m/z* 250 (12%, $[M+1]^+$), 249 (48, $[M]^+$), 248 (100, $[M-1]^+$).

3-(Methoxymethyl)-1-methyl-4-pentyl-2(*1H*)-quinolinone (**3ah**)



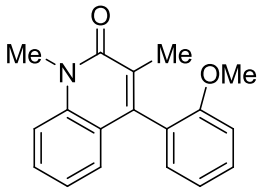
Isolated by column chromatography (silica gel, hexane/AcOEt = 2/1). Pale yellow oil, 90.4 mg, 66% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J = 8.2, 1.3 Hz, 1H), 7.54 (dt, J = 7.9, 1.3 Hz, 1H), 7.34 (d, J = 7.7 Hz, 1H), 7.24 (dt, J = 7.7, 0.9 Hz, 1H), 4.64 (s, 2H) 3.73 (s, 3H), 3.46 (s, 3H), 2.95-2.99 (m, 2H), 1.61-1.71 (m, 2H), 1.35-1.52 (m, 4H), 0.93 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.0, 150.3, 139.6, 130.2, 126.0, 125.5, 121.8, 120.2, 114.3, 66.2, 58.4, 32.2, 30.0, 29.7, 28.8, 22.3, 13.9. IR (neat): 2923.9, 1635.5, 1091.6, 750.3 cm^{-1}. EI-MS: *m/z* 274 (2%, $[M+1]^+$), 273 (2, $[M]^+$), 258 (100), 243 (8), 228 (6). EI-HRMS: Calcd. for $C_{17}H_{23}NO_2$ ($[M]^+$), 273.1729. Found, 273.1729.

4-(Methoxymethyl)-1-methyl-3-pentyl-2(*1H*)-quinolinone (**3ah'**)



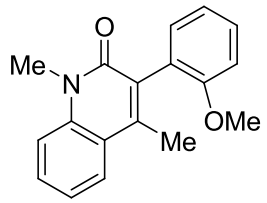
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). Pale yellow solids, 34.4 mg, 25% yield: m.p. 48-50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.2 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.25 (t, J = 7.7 Hz, 1H), 4.72 (s, 2H), 3.75 (s, 3H), 3.47 (s, 3H), 2.80-2.86 (m, 2H), 1.49-1.59 (m, 2H), 1.33-1.47 (m, 4H), 0.91 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.1, 139.1, 138.7, 134.3, 129.3, 125.7, 122.0, 120.3, 114.0, 67.7, 58.5, 32.0, 30.0, 29.6, 27.7, 22.5, 14.0. IR (KBr): 2927.7, 1635.5, 1596.9, 1099.3 cm^{-1}. EI-MS: *m/z* 274 (11%, $[M+1]^+$), 273 (14, $[M]^+$), 258 (100), 228 (96), 202 (72). EI-HRMS: Calcd. for $C_{17}H_{23}NO_2$ ($[M]^+$), 273.1729. Found, 273.1728.

4-(2-Methoxyphenyl)-1,3-dimethyl-2(*1H*)-quinolinone (**3ai**)



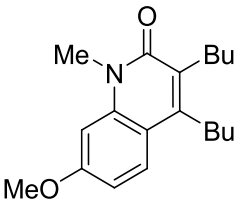
Isolated by column chromatography (silica gel, hexane/AcOEt = 2/1). White solids, 75.4 mg, 54% yield: m.p. 144-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.49 (m, 2H), 7.37 (d, J = 8.2 Hz, 1H), 7.03-7.09 (m, 5H), 3.80 (s, 3H), 3.70 (s, 3H), 2.01 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 50 ºC): δ 162.6, 156.5, 143.6, 138.5, 130.3, 129.6, 129.0, 128.4, 127.1, 125.5, 121.6, 121.4, 120.7, 113.8, 111.1, 55.5, 29.8, 15.0. IR (KBr): 1641.3, 1253.6, 750.3 cm^{-1}. EI-MS: *m/z* 280 (15%, $[M+1]^+$), 279 (73, $[M]^+$), 264 (41), 248 (100). EI-HRMS: Calcd. for $C_{18}H_{17}NO_2$ ($[M]^+$), 279.1259. Found, 279.1259.

3-(2-Methoxyphenyl)-1,4-dimethyl-2(*1H*)-quinolinone (**3ai'**)



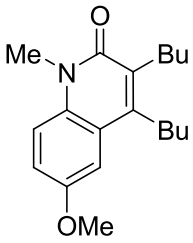
Isolated by column chromatography (silica gel, hexane/AcOEt = 1/1). White solids, 21.0 mg, 15%: m.p. 52-53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (ddd, J = 8.2, 1.4, 0.5 Hz, 1H), 7.57 (dt, J = 7.9, 1.4 Hz, 1H), 7.39 (dd, J = 8.6, 0.9 Hz, 1H), 7.31-7.37 (m, 1H), 7.27 (dt, J = 7.7, 0.9 Hz, 1H), 7.14 (dd, J = 7.3, 1.8 Hz, 1H), 7.03 (dt, J = 7.7, 0.9 Hz, 1H), 6.99 (d, J = 8.2 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 2.26 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.3, 157.1, 143.2, 139.3, 131.2, 129.9, 129.3, 219.1, 125.7, 125.5, 121.7, 121.5, 120.6, 114.2, 111.0, 55.6, 29.8, 16.6. IR (KBr): 1637.5, 1247.9, 750.3 cm^{-1}. EI-MS: *m/z* 280 (3%, $[M+1]^+$), 279 (17, $[M]^+$), 264 (26), 248 (100). EI-HRMS: Calcd. for $C_{18}H_{17}NO_2$ ($[M]^+$), 279.1259. Found, 279.1263.

3,4-Dibutyl-7-methoxy-1-methyl-2(*1H*)-quinolinone (**3ba**)



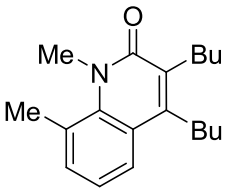
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 128 mg, 85% yield: m.p. 100-101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 9.1 Hz, 1H), 6.82 (dd, J = 9.1, 2.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 3.89 (s, 3H), 3.69 (s, 3H), 2.82 (t, J = 7.2 Hz, 2H), 2.69 (t, J = 7.2 Hz, 2H), 1.40-1.63 (m, 8H), 1.00 (t, J = 6.9 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.5, 160.2, 144.9, 140.2, 128.2, 126.2, 114.6, 108.8, 98.5, 55.3, 32.1, 31.4, 29.6, 28.4, 27.4, 23.09, 23.06, 13.9, 13.7. IR (KBr): 2956.7, 1618.2 cm^{-1}. EI-MS: *m/z* 302 (3%, $[M+1]^+$), 301 (19, $[M]^+$), 272 (26), 244 (38), 217 (51), 18 (100). Anal. Calcd. for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03. Found: C, 75.43; H, 9.04.

3,4-Dibutyl-6-methoxy-1-methyl-2(*1H*)-quinolinone (**3ca**)



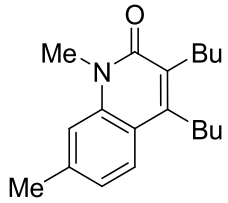
Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 134.4 mg, 89% yield: m.p. 51-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J = 9.1 Hz, 1H), 7.11 (d, J = 2.7 Hz, 1H), 7.02 (dd, J = 9.1, 2.7 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 3H), 2.78 (t, J = 7.7 Hz, 2H), 2.66 (t, J = 7.7 Hz, 2H), 1.36-1.57 (m, 8H), 0.94 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.4, 154.2, 144.1, 133.1, 131.8, 121.2, 116.1, 115.1, 108.1, 55.3, 31.6, 31.3, 29.5, 28.3, 27.7, 23.01, 22.98, 13.8, 13.6. IR (KBr): 2956.7, 1637.5, 806.2 cm^{-1}. EI-MS: *m/z* 302 (8%, $[M+1]^+$), 301 (29, $[M]^+$), 272 (38), 244 (100), 217 (88). EI-HRMS: Calcd. for $C_{19}H_{27}NO_2$ ($[M]^+$), 301.2042. Found, 301.2041.

3,4-Dibutyl-1,8-dimethyl-2(*1H*)-quinolinone (**3da**)



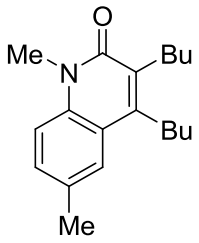
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). Pale yellow oil, 123 mg, 86% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.7 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 3.74 (s, 3H), 2.82 (t, J = 7.2 Hz, 2H), 2.70 (t, J = 7.2 Hz, 2H), 2.61 (s, 3H), 1.38-1.61 (m, 8H), 0.93-0.99 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.3, 145.2 140.3, 133.2, 130.7, 124.8, 122.7, 122.3, 121.9, 37.5, 31.9, 31.3, 28.6, 27.5, 23.6, 23.11, 23.06, 13.9, 13.8. IR (KBr): 2956.7, 1633.6, 771.5 cm^{-1}. EI-MS: *m/z* 286 (7%, $[M+1]^+$), 285 (20, $[M]^+$), 256 (52), 242 (69), 228 (100). Anal. Calcd. for $C_{19}H_{27}NO$: C, 79.95; H, 9.53. Found: C, 79.65; H, 9.29.

3,4-Dibutyl-1,7-dimethyl-2(*1H*)-quinolinone (**3ea**)



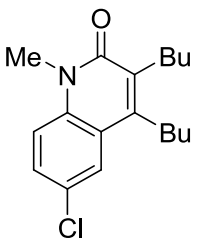
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). White solids, 133 mg, 93% yield: m.p. 83-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.6 Hz, 1H), 7.12 (s, 1H), 7.03 (d, J = 8.2 Hz, 1H), 3.71 (s, 3H), 2.83 (t, J = 7.2 Hz, 2H), 2.71 (t, J = 7.2 Hz, 2H), 2.46 (s, 3H), 1.42-1.62 (m, 8H), 0.99 (t, J = 7.7 Hz, 3H), 0.97 (t, J = 7.7 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 144.9, 139.2, 138.7, 130.0, 124.6, 122.9, 118.2, 114.4, 32.0, 31.4, 29.5, 28.3, 27.5, 23.08, 23.06, 21.67, 13.8, 13.7. IR (KBr): 2954.7, 1635.5, 825.5 cm^{-1}. EI-MS: *m/z* 286 (5%, $[M+1]^+$), 285 (20, $[M]^+$), 256 (22), 228 (50), 201 (100). Anal. Calcd. for $C_{19}H_{27}NO$: C, 79.95; H, 9.53. Found: C, 79.72; H, 9.70.

3,4-Dibutyl-1,6-dimethyl-2(*1H*)-quinolinone (**3fa**)



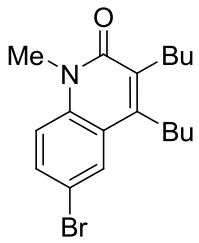
Isolated by column chromatography (silica gel, hexane/AcOEt = 7/2). Pale yellow oil, 130 mg, 91% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (brs, 1H), 7.28 (dd, J = 8.6, 2.3 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 3.70 (s, 3H), 2.85 (t, J = 7.2 Hz, 2H), 2.74 (t, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.42-1.65 (m, 8H), 1.01 (t, J = 6.8 Hz, 3H), 0.98 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.9, 144.6, 136.6, 131.2, 130.8, 130.0, 124.6, 120.4, 114.0, 31.9, 31.3, 29.5, 28.2, 27.7, 23.08, 23.06, 20.9, 13.8, 13.7. IR (neat): 2927.7, 1635.5, 804.3 cm^{-1}. EI-MS: *m/z* 286 (7%, $[M+1]^+$), 285 (27, $[M]^+$), 256 (46), 228 (72), 201 (100). Anal. Calcd. for $C_{19}H_{27}NO$: C, 79.95; H, 9.53. Found: C, 79.68; H, 9.54.

3,4-Dibutyl-6-chloro-1-methyl-2(*1H*)-quinolinone (**3ga**)



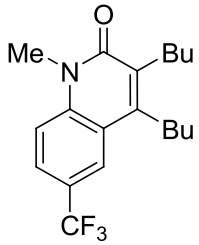
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). White solids, 133 mg, 87% yield: m.p. 44-45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 2.7 Hz, 1H), 7.40 (dd, J = 9.1, 2.7 Hz, 1H), 7.24 (d, J = 9.1 Hz, 1H), 3.70 (s, 3H), 2.81 (t, J = 7.2 Hz, 2H), 2.71 (t, J = 7.2 Hz, 2H), 1.42-1.63 (m, 8H), 1.01 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 143.8, 137.2, 132.6, 128.7, 127.1, 124.2, 121.7, 115.4, 31.7, 31.2, 29.7, 28.2, 27.7, 23.1, 23.0, 13.8, 13.7. IR (KBr): 2956.7, 1633.6, 808.1 cm^{-1}. EI-MS: *m/z* 307 (6%, $[M+2]^+$), 306 (10, $[M+1]^+$), 305 (28, $[M]^+$), 276 (47), 248 (77), 221 (100). Anal. Calcd. for $C_{18}H_{24}ClNO$: C, 70.69; H, 7.91. Found: C, 70.49; H, 8.00.

6-Bromo-3,4-dibutyl-1-methyl-2(*1H*)-quinolinone (**3ha**)



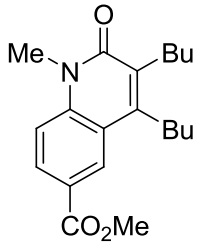
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1 then CH_2Cl_2). White solids, 99.0 mg, 57% yield: m.p. 59-60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.52 (d, J = 9.1 Hz, 1H), 7.17 (d, J = 9.1 Hz, 1H), 3.77 (s, 3H), 2.79 (t, J = 6.8 Hz, 2H), 2.69 (t, J = 6.8 Hz, 2H), 1.38-1.61 (m, 8H), 0.92-1.02 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.7, 143.9, 137.7, 132.7, 131.6, 127.3, 122.3, 115.8, 114.7, 31.9, 31.3, 29.8, 28.3, 27.8, 23.14, 23.09, 13.9, 13.8. IR (KBr): 2954.7, 1635.5, 817.8 cm^{-1}. EI-MS: *m/z* 351 (6%, $[M+2]^+$), 350 (3, $[M+1]^+$), 349 (6, $[M]^+$), 320 (10), 292 (100), 265 (23). Anal. Calcd. for $C_{18}H_{24}BrNO$: C, 61.72; H, 6.91. Found: C, 61.58; H, 6.94.

3,4-Dibutyl-1-methyl-6-(trifluoromethyl)-2(*1H*)-quinolinone (**3ia**)



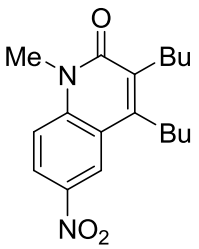
Isolated by column chromatography (silica gel, hexane/AcOEt = 5/1). White solids, 139 mg, 82% yield: m.p. 48-49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (brs, 1H), 7.71 (dd, J = 9.1, 1.8 Hz, 1H), 7.43 (d, J = 9.1 Hz, 1H), 3.76 (s, 3H), 2.90 (t, J = 7.2 Hz, 2H), 2.74 (t, J = 7.2 Hz, 2H), 1.43-1.64 (m, 8H), 1.03 (t, J = 7.2 Hz, 3H), 0.98 (d, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.0, 144.6, 140.1, 132.9, 125.3 (q, $^3J_{C\text{-}F}$ = 23.9 Hz), 123.7 (q, $^2J_{C\text{-}F}$ = 32.5 Hz), 124.2 (q, $^1J_{C\text{-}F}$ = 273 Hz), 122.2 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 120.3, 114.6, 31.9, 31.2, 29.9, 28.2, 27.8, 23.1, 23.0, 13.8, 13.7. IR (KBr): 2956.7, 1647.1, 1112.9, 819.7 cm^{-1}. EI-MS: *m/z* 351 (6%, $[M+2]^+$), 350 (3, $[M+1]^+$), 349 (6, $[M]^+$), 320 (10), 292 (100), 265 (23). Anal. Calcd. for $C_{19}H_{24}F_3NO$: C, 67.24; H, 7.13. Found: C, 67.03; H, 7.13.

3,4-Dibutyl-1,2-dihydro-1-methyl-2-oxo-6-quinolinecarboxylic acid methyl ester (**3ja**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 131 mg, 80% yield: m.p. 83-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 1.8 Hz, 1H), 8.04 (dd, J = 8.6, 1.8 Hz, 1H), 7.28 (d, J = 8.6 Hz, 1H), 3.90 (s, 3H), 3.68 (s, 3H), 2.85 (t, J = 6.8 Hz, 2H), 2.66 (t, J = 6.8 Hz, 2H), 1.37-1.50 (m, 8H), 0.97 (t, J = 6.8 Hz, 3H), 0.92 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.5, 162.0, 145.2, 141.7, 132.0, 129.6, 127.0, 123.2, 120.0, 114.0, 52.0, 32.0, 31.2, 29.8, 28.2, 27.7, 23.05, 23.00, 13.8, 13.7. IR (KBr): 2958.6, 1718.5, 1637.5, 1242.1 cm^{-1}. EI-MS: *m/z* 330 (2%, $[M+1]^+$), 329 (7, $[M]^+$), 314 (5), 300 (41), 272 (73), 245 (68), 18 (100). EI-HRMS: Calcd. for $C_{20}H_{27}NO_3$ ($[M]^+$), 329.1991. Found, 329.1988.

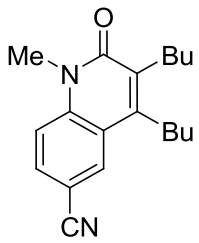
3,4-Dibutyl-1-methyl-6-nitro-2(*1H*)-quinolinone (**3ka**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 3/1). White solids, 116 mg, 73% yield: m.p. 69-70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, J = 2.7 Hz, 1H), 8.33 (dd, J = 9.5, 2.7 Hz, 1H), 7.45 (d, J = 9.5 Hz, 1H), 3.80 (s, 3H), 2.93 (d, J = 7.2 Hz, 2H), 2.74 (d, J = 7.2 Hz, 2H), 1.42-1.69 (m, 8H), 1.04 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.8, 144.8, 142.8, 141.9, 133.6, 123.6, 121.0, 120.3, 114.7, 31.9, 31.1, 30.2, 28.3, 27.8, 23.03, 23.00, 13.8, 13.7. IR (KBr): 2931.6, 1643.2, 1606.6, 1338.5, 736.8 cm^{-1}. EI-MS: *m/z*

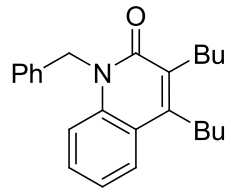
317 (2%, $[M+1]^+$), 316 (6, $[M]^+$), 299 (6), 287 (50), 259 (100), 232 (74). Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65. Found: C, 68.07; H, 7.13.

3,4-Dibutyl-1,2-dihydro-1-methyl-2-oxo-6-quinolinecarbonitrile (**3la**)



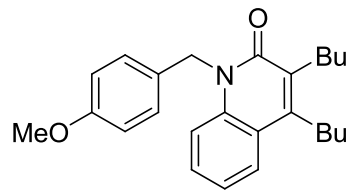
Isolated by column chromatography (silica gel, hexane/AcOEt = 4/1). White solids, 87.5 mg, 59% yield: m.p. 108-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 1.4 Hz, 1H), 7.73 (dd, J = 7.2, 1.4 Hz, 1H), 7.42 (d, J = 1.4 Hz, 1H), 3.75 (s, 3H), 2.86 (d, J = 8.2 Hz, 2H), 2.72 (d, J = 8.2 Hz, 2H), 1.41-1.63 (m, 8H), 1.03 (t, J = 6.8 Hz, 3H), 0.97 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.8, 144.1, 141.4, 133.4, 131.5, 129.6, 120.8, 119.0, 115.0, 105.1, 31.9, 31.1, 30.0, 28.3, 27.7, 23.09, 23.06, 13.83, 13.75. IR (KBr): 2954.7, 1637.5, 1083.9 cm^{-1}. EI-MS: *m/z* 297 (2%, $[M+1]^+$), 296 (8, $[M]^+$), 267 (30), 239 (57), 212 (56), 18 (100). Anal. Calcd. for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16. Found: C, 76.91; H, 8.24.

3,4-Dibutyl-1-(phenylmethyl)-2(*1H*)-quinolinone (**3ma**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 8/1). White solids, 153 mg, 88% yield: m.p. 51-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.2 Hz, 1H), 7.04-7.23 (m, 8H), 5.47 (s, 2H), 2.80 (t, J = 7.7 Hz, 2H), 2.69 (t, J = 7.7 Hz, 2H), 1.35-1.58 (m, 8H), 0.92 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 145.5, 138.2, 136.8, 131.3, 128.9, 128.6, 126.9, 126.5, 124.9, 121.7, 120.8, 115.0, 46.2, 32.0, 31.4, 28.5, 27.7, 23.22, 23.18, 13.9, 13.8. IR (KBr): 2954.7, 1635.5, 754.1 cm^{-1}. EI-MS: *m/z* 348 (3%, $[M+1]^+$), 347 (7, $[M]^+$), 290 (12), 263 (14), 91 (100). Anal. Calcd. for $C_{24}H_{29}NO$: C, 82.95; H, 8.41. Found: C, 82.96; H, 8.54.

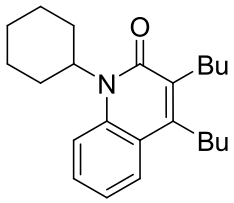
3,4-Dibutyl-1-[(4-methoxyphenyl)methyl]-2(*1H*)-quinolinone (**3na**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 10/1). White solids, 124 mg, 66% yield: m.p. 112-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.2 Hz, 1H), 7.27-7.24 (m, 2H), 7.13-7.18 (m, 3H), 6.80 (d, J = 8.6 Hz, 2H), 5.50 (s, 2H), 3.72 (s, 3H), 2.89 (t, J = 7.7 Hz, 2H), 2.78 (t, J = 7.7 Hz, 2H), 1.43-1.68 (m, 8H), 1.02 (t, J = 7.2 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 158.5, 145.5, 138.2, 131.3, 128.89, 128.86, 127.9, 124.9, 121.6, 120.8, 115.0, 114.0, 55.1, 45.7, 32.0,

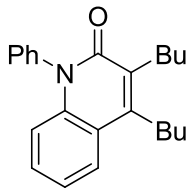
31.4, 28.5, 27.7, 23.22, 23.19, 13.9, 13.8. IR (KBr): 2929.7, 1635.5, 767.6 cm^{-1}. EI-MS: *m/z* 378 (6%, $[M+1]^+$), 377 (21, $[M]^+$), 256 (18), 121 (100). Anal. Calcd. for $C_{25}H_{31}NO_2$: C, 79.54; H, 8.28. Found: C, 79.27; H, 8.39.

3,4-Dibutyl-1-cyclohexyl-2(*1H*)-quinolinone (**3oa**)



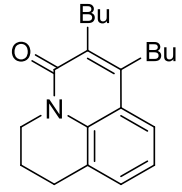
Isolated by column chromatography (silica gel, hexane/AcOEt = 15/1). Colorless oil, 138 mg, 81% yield: ^1H NMR (400 MHz, $CDCl_3$, 50 ºC): δ 7.70 (d, J = 7.6 Hz, 1H), 7.69 (brs, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 4.88 (br, 1H), 2.86 (m, 2H), 2.68-2.71 (m, 4H), 1.92 (d, J = 12 Hz, 2H), 1.73-1.79 (m, 3H), 1.30-1.62 (m, 11H), 0.93-1.02 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 50 ºC): δ 162.7, 144.4, 138.7, 132.3, 128.1, 125.1, 121.5, 121.1, 114.8, 57.1, 31.9, 31.5, 29.0, 28.5, 27.8, 26.7, 25.6, 23.2, 23.2, 13.9, 13.8. IR (neat): 2931.6, 1633.6, 732.9 cm^{-1}. EI-MS: *m/z* 340 (17%, $[M+1]^+$), 339 (55, $[M]^+$), 338 (18, $[M-1]^+$), 257 (100), 200 (95), 173 (91). EI-HRMS: Calcd. for $C_{23}H_{33}NO$ ($[M+H]^+$), 339.2562. Found, 339.2562.

3,4-Dibutyl-1-phenyl-2(*1H*)-quinolinone (**3pa**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 7/1). Pale yellow oil, 147 mg, 88% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 7.7 Hz, 1H), 7.05-7.19 (m, 4H), 6.56 (d, J = 8.2 Hz, 1H), 2.85 (t, J = 8.4 Hz, 2H), 2.65 (t, J = 8.4 Hz, 2H), 1.32-1.64 (m, 8H), 0.94 (t, J = 7.2 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.1, 145.8, 139.7, 138.4, 131.8, 129.9, 128.8, 128.5, 128.4, 124.5, 121.9, 120.3, 116.1, 32.0, 31.3, 28.6, 27.5, 23.23, 23.17, 13.84, 13.82. IR (KBr): 2956.7, 1645.2, 752.2 cm^{-1}. EI-MS: *m/z* 334 (6%, $[M+1]^+$), 333 (14, $[M]^+$), 304 (38), 276 (89), 249.(100). EI-HRMS: Calcd. for $C_{23}H_{27}NO$ ($[M]^+$), 333.2093. Found, 3333.2095.

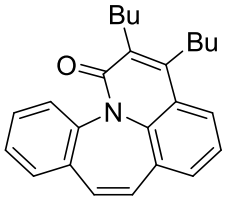
6,7-Dibutyl-2,3-dihydro-*1H*,*5H*-benzo[*ij*]quinolizin-5-one (**3qa**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 8/1). White solids, 75.8 mg, 51% yield: m.p. 47-48 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.2 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.11 (d, J = 7.7 Hz, 1H), 4.21 (t, J = 5.9 Hz, 2H), 2.96 (t, J = 6.3 Hz, 2H), 2.86 (t, J = 7.2 Hz, 2H), 2.73 (t, J = 6.8 Hz, 2H), 2.04-2.13 (m, 2H), 1.42-1.66 (m, 8H), 1.00 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.6, 144.9, 135.4, 130.9, 128.4, 124.7, 122.8, 121.1, 120.4, 42.5, 32.0, 31.4, 28.5, 28.0, 27.5,

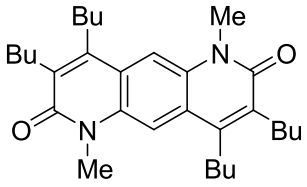
23.18, 23.16, 20.7, 13.9, 13.8. IR (KBr): 2954.7, 1631.7, 773.4 cm^{-1}. EI-MS: *m/z* 298 (6%, $[M+1]^+$), 297 (24, $[M]^+$), 268 (71), 240 (96), 213 (100). Anal. Calcd. for $C_{20}H_{27}NO$: C, 80.76; H, 9.15. Found: C, 80.49; H, 9.05.

2,3-Dibutyl-*1H*-benzo[*b*]pyrido[3,2,1-*jk*][1]benzazepin-1-one (**3ra**)



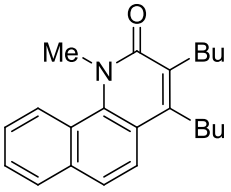
Isolated by column chromatography (silica gel, hexane/CH_2Cl_2 = 2/1). Pale yellow oil, 125 mg, 70% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, J = 8.2, 1.4 Hz, 1H), 7.26 (dt, J = 7.2, 1.8 Hz, 1H), 7.10-7.21 (m, 3H), 7.05 (d, J = 7.7 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.69 (d, J = 11.8 Hz, 1H), 6.46 (d, J = 11.8 Hz, 1H), 2.81 (t, J = 8.2 Hz, 2H), 2.68-2.75 (m, 2H), 1.41-1.70 (m, 8H), 1.01 (t, J = 6.8 Hz, 3H), 0.97 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.2, 146.4, 146.0, 142.4, 134.7, 133.8, 133.1, 130.9, 130.7, 129.6, 129.5, 129.2, 128.1, 126.9, 123.7, 123.6, 123.0, 31.6, 31.4, 28.6, 27.4, 23.15, 23.09, 13.9, 13.8. IR (KBr): 2927.7, 1635.5, 754.1 cm^{-1}. EI-MS: *m/z* 358 (11%, $[M+1]^+$), 357 (46, $[M]^+$), 328 (26), 300 (70), 273 (28), 18 (100). EI-HRMS: Calcd. for $C_{25}H_{27}NO$ ($[M]^+$), 357.2093. Found, 357.2088.

3,4,8,9-Tetrabutyl-1,6-dihydro-1,6-dimethyl-pyrido[2,3-*g*]quinoline-2,7-dione (**3sa**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 5/1). Yellow solids, 78.5 mg, 68% yield: m.p. 196-197 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 2H), 3.80 (s, 6H), 2.95 (t, J = 7.7 Hz, 4H), 2.77 (t, J = 7.7 Hz, 4H), 1.46-1.73 (m, 16H), 1.05 (t, J = 7.2 Hz, 6H), 0.99 (t, J = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.7, 143.8, 133.9, 133.3, 121.6, 109.2, 31.7, 31.5, 29.6, 28.4, 28.0, 23.1, 13.89, 13.84. IR (KBr): 2956.7, 1627.8 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 466 (26%, $[M+2]^+$), 465 (100, $[M+1]^+$), 225 (4). EI-HRMS: Calcd. for $C_{30}H_{44}N_2O_2$ ($[M]^+$), 464.3403. Found, 464.3400.

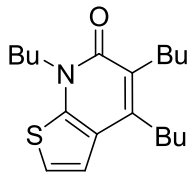
3,4-Dibutyl-1-methyl-benzo[*h*]quinolin-2(*1H*)-one (**3ta**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 6/1). Pale yellow solids, 145 mg, 90% yield: m.p. 58-59 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 9.1 Hz, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.42-7.53 (m, 2H), 4.00 (s, 3H), 2.91 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H), 1.45-1.67 (m, 8H), 0.98-1.03 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.6, 145.6, 137.8, 134.4, 130.6, 128.1, 126.4, 125.5, 124.5, 123.8, 123.0, 121.6, 118.4, 40.7,

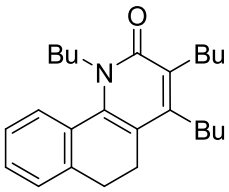
32.1, 31.3, 28.7, 27.4, 23.1, 23.1, 13.9, 13.8. IR (KBr): 2956.7, 1629.7, 1612.4 cm^{-1}. EI-MS: *m/z* 322 (13%, $[M+1]^+$), 321 (50, $[M]^+$), 292 (51), 278 (68), 264 (100), 237 (56). EI-HRMS: Calcd. for $C_{22}H_{27}NO$ ($[M]^+$), 321.2093. Found, 321.2090.

4,5,7-Tributyl-thieno[2,3-*b*]pyridin-6(*7H*)-on (**3ua**)



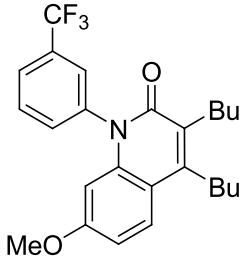
Isolated by column chromatography (silica gel, hexane/AcOEt = 10/1). Pale yellow oil, 158 mg, 99% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, J = 5.9 Hz, 1H), 6.91 (d, J = 5.9 Hz, 1H), 4.12 (t, J = 7.7 Hz, 2H), 2.75 (t, J = 7.7 Hz, 2H), 2.63 (t, J = 7.7 Hz, 2H), 1.77-1.85 (m, 2H), 1.54-1.63 (m, 2H), 1.39-1.53 (m, 8H), 0.94-1.00 (m, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.0, 144.9, 144.7, 126.9, 122.5, 120.9, 114.9, 48.7, 32.1, 31.4, 30.5, 29.1, 27.0, 23.13, 23.06, 20.3, 13.9, 13.8, 13.7. IR (KBr): 2956.7, 1633.6, 1533.3, 729.0 cm^{-1}. EI-MS: *m/z* 320 (11%, $[M+1]^+$), 319 (45, $[M]^+$), 302 (29), 290 (41), 262 (89), 235 (84), 220 (44), 28 (100). Anal. Calcd. for $C_{19}H_{29}NOS$: C, 71.42; H, 9.15. Found: C, 71.59; H, 9.34.

1,3,4-Tributyl-5,6-dihydro-benzo[*h*]quinolin-2(*1H*)-one (**3va**)



Isolated by column chromatography (silica gel, hexane/AcOEt = 10/1). Pale yellow oil, 94.4 mg, 52% yield: ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.2 Hz, 1H), 7.20-7.29 (m, 3H), 4.28 (t, J = 7.2 Hz, 2H), 2.70 (t, J = 7.2 Hz, 2H), 2.65 (t, J = 7.2 Hz, 2H), 2.47-2.56 (m, 4H), 1.73-1.82 (m. 2H), 1.41-1.60 (m, 8H), 1.18-1.27 (m, 2H), 0.97 (t, J = 7.2 Hz, 6H), 0.83 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.7, 147.3, 139.8, 139.1, 130.3, 129.7, 127.7, 127.3, 125.9, 119.4, 48.2, 31.7, 31.4, 30.8, 29.3, 29.2, 27.4, 24.6, 23.2, 23.1, 19.8, 13.9, 13.8, 13.5. IR (KBr): 2956.7, 1633.6, 1533.3, 729.0 cm^{-1}. EI-MS: *m/z* 366 (13%, $[M+1]^+$), 365 (100, $[M]^+$), 348 (39), 322 (37), 281 (25), 225 (29). EI-HRMS: Calcd. for $C_{25}H_{35}NO$ ($[M]^+$), 365.2719. Found, 365.2708.

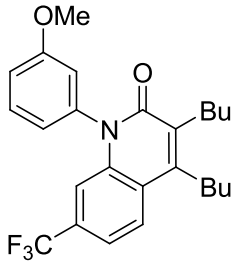
3,4-Dibutyl-7-methoxy-1-[3-(trifluoromethyl)phenyl]-2(*1H*)-quinolinone (**3wa**)



Isolated by column chromatography (silica gel, toluene/AcOEt = 50/1). White solids, 184 mg, 85% yield: m.p. 126-127 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.68-7.77 (m, 3H), 7.59 (s, 1H), 7.51 (d, J = 7.7 Hz, 1H), 6.82 (dd, J = 9.1, 2.3 Hz, 1H), 6.03 (d, J = 2.3 Hz, 1H), 3.66 (s, 3H), 2.91 (t, J = 7.7 Hz, 2H), 2.71 (t, J = 7.7 Hz, 2H), 1.42-1.70 (m, 8H), 1.04 (t, J = 7.2 Hz, 3H), 0.96 (t, J = 7.7 Hz,

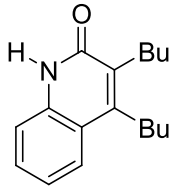
3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.5, 160.0, 146.5, 140.9, 139.0, 132.7, 132.4 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 130.6, 128.6, 126.3, 126.2 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.4 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.5 (q, $^1J_{C\text{-}F}$ = 272 Hz), 114.6, 109.4, 100.2, 55.15, 55.12, 32.1, 31.4, 28.7, 27.2, 23.2, 23.1, 13.8. IR (KBr): 2960.5, 1647.1 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 432 (100%, $[M+1]^+$), 431 (3, $[M]^+$). Anal. Calcd. for $C_{25}H_{28}F_3NO_2$: C, 69.59; H, 6.54. Found: C, 69.68; H, 6.54.

3,4-Dibutyl-1-(3-methoxyphenyl)-7-(trifluoromethyl)-2(*1H*)-quinolinone (**3wa'**)



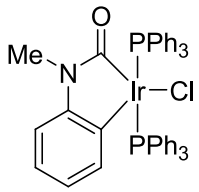
Isolated by column chromatography (silica gel, toluene/AcOEt = 40/1). White solids, 10.2 mg, 5% yield: m.p. 89-90 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.6 Hz, 1H), 7.51 (t, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.07 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.94 (s, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.78 (t, *J* = 2.3 Hz, 1H), 3.83 (s, 3H), 2.94 (t, *J* = 7.7 Hz, 2H), 2.75 (t, *J* = 7.3 Hz, 2H), 1.41-1.72 (m, 8H), 1.04 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.9, 161.2, 145.2, 139.6, 138.6, 134.3, 131.1, 130.3 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 125.4, 123.7 (q, $^1J_{C\text{-}F}$ = 273 Hz), 122.7, 120.7, 118.2 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 115.1, 114.1, 113.1 (q, $^3J_{C\text{-}F}$ = 4.8 Hz), 55.4, 31.9, 31.2, 28.7, 27.7, 23.27, 23.24, 13.90, 13.88. IR (KBr): 2958.6, 1652.9, 1122.5 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 432 (100%, $[M+1]^+$), 431 (81, $[M]^+$). EI-HRMS: Calcd. for $C_{25}H_{28}F_3NO_2$ ($[M]^+$), 431.2072. Found, 431.2074.

3,4-Dibutyl-2(1*H*)-quinolone



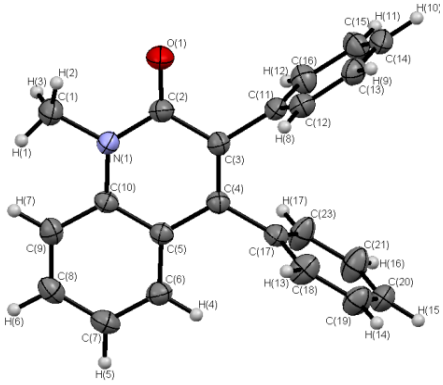
Isolated by column chromatography (silica gel, hexane/AcOEt = 1/1). White solids, 35.1 mg, 91% yield: m.p. 134-135 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 12.2 (s, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.38-7.45 (m, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 2.90 (t, *J* = 7.7 Hz, 2H), 2.78 (t, *J* = 7.2 Hz, 2H), 1.47-1.66 (m, 8H), 0.97-1.04 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.0, 147.4, 137.3, 131.3, 128.9, 124.2, 122.0, 120.1, 116.3, 32.1, 31.6, 28.6, 26.7, 23.3, 23.1, 14.1, 13.9. IR (KBr): 2954.7, 1654.8, 759.9 cm^{-1}. EI-MS: *m/z* 258 (2%, $[M+1]^+$), 257 (9, $[M]^+$), 240 (10), 228 (29), 200 (55), 173 (71), 18 (100). EI-HRMS: Calcd. for $C_{17}H_{23}NO$ ($[M]^+$), 257.1780. Found, 257.1777.

Iridium complex (**4**)

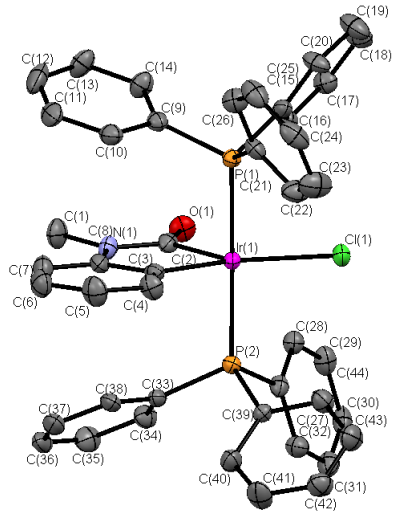


Yellow solids, 30.5 mg, 69% yield: 290-291 °C (decomp.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.55 (m, 30H), 7.16 (d, J = 7.2 Hz, 1H), 6.68 (t, J = 7.7 Hz, 1H), 6.18 (t, J = 7.2 Hz, 1H), 5.62 (d, J = 7.2 Hz, 1H), 1.67 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.1 (t, $J_{C\text{-}P}$ = 6.7 Hz), 150.1, 134.6 (t, $J_{C\text{-}P}$ = 5.7 Hz), 132.7, 130.1, 129.2 (t, $J_{C\text{-}P}$ = 26.7 Hz), 127.8 (t, $J_{C\text{-}P}$ = 4.8 Hz), 122.9 (t, $J_{C\text{-}P}$ = 7.6 Hz), 122.5, 117.3, 109.0, 26.1. ^{31}P{^{1}H} NMR (160 MHz, $CDCl_3$): δ 20.3. IR (KBr): 3055.0, 1618.2, 1434.9, 1097.4, 742.5, 520.7 cm^{-1}. MALDI-TOF-MS (DIT): *m/z* 885 (1%, $[M]^+$), 850 (100, $[M–Cl]^+$). Anal. Calcd. for $C_{44}H_{37}ClIrNOP_2 \cdot 0.5CH_2Cl_2$: C, 57.60; H, 4.13. Found: C, 57.33; H, 4.04.

X-ray Diffraction Studies of 3ac and 4



Single crystal of **3ac** was obtained by recrystallization from hot hexane solution. Crystal data for **3ac**: $C_{22}H_{17}NO$, M = 311.38, triclinic, space group = P_1 (#2), a = 9.335 (5) Å, b = 9.749(5) Å, c = 10.565(5) Å, α = 65.996(19)°, β = 67.20(2)°, γ = 79.05(2)°, V = 809.1(7) Å^3, Z = 2, density (calc.) = 1.278, total reflections collected = 6191, unique reflections = 3479 (R_{int} = 0.039), GOF = 1.004. The final $R1$ factor was 0.0656 ($I>2\sigma(I)$) ($wR2$ = 0.1732, all data).



Single crystal of **4** was obtained by slow evaporation from CH_2Cl_2/hexane solution. Crystal data for **4**: $C_{44}H_{37}ClIrNOP_2$, M = 885.40, monoclinic, space group = $P2_1/n$ (#14), a = 14.3648(8) Å, b = 10.2095(3) Å, c = 25.0281(12) Å, β = 100.934(2)°, V = 3603.9(3) Å^3, Z = 4, density (calc.) = 1.632, total reflections collected = 26008, unique reflections = 8195 (R_{int} = 0.051), GOF = 1.003. The final $R1$ factor was 0.0327 ($I>2\sigma(I)$) ($wR2$ = 0.0645, all data).

4-5. References and Notes

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(2) For selected examples, see; (a) Guimond, N.; Gouliaras, C.; Fagnou, K. *J. Am. Chem. Soc*. **2010**, *132*, 6908–6909. (b) Perreault, S.; Rovis, T. *Chem. Soc. Rev.* **2009**, *38*, 3149–3159. (c) Satoh, T.; Ueura, K.; Miura, M. *Pure Appl. Chem*. **2008**, *80*, 1127–1134.

(3) (a) Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc*. **2009**, *131*, 7494–7495. (b) Kajita, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc*. **2008**, *130*, 17226–17227. (c) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett*. **2008**, *10*, 3085–3088. (d) Kajita, Y.; Matsubara, S.; Kurahashi, T. *J. Am. Chem. Soc*. **2008**, *130*, 6058–6059.

(4) For recent reviews of carbonylative annulations by using carbon monoxide as a carbonyl source, see: (a) Chatani, N. *Chem. Rec*. **2008**, *8*, 201–212. (b) Zeni, G.; Larock, R. C. *Chem. Rev*. **2006**, *106*, 4644–4680. (c) Vasapollo, G.; Mele, G. *Cur. Org. Chem.* **2006**, *10*, 1397–1421. (d) Vizer, S. A.; Yerzhanov, K. B.; Al Quntar, A. A. A.; Dembitsky, V. M. *Tetrahedron* **2004**, *60*, 5499–5538.

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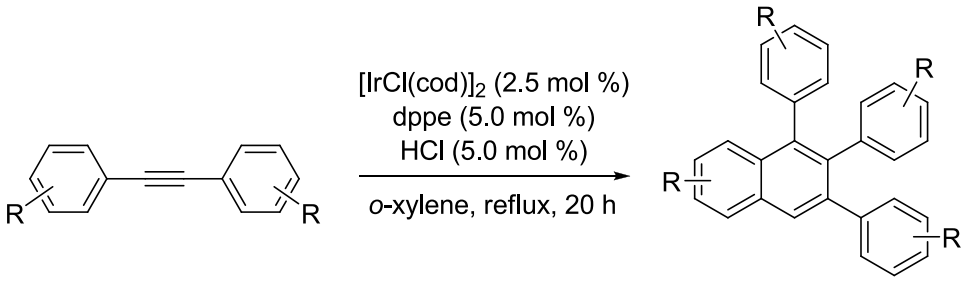
Chapter 5

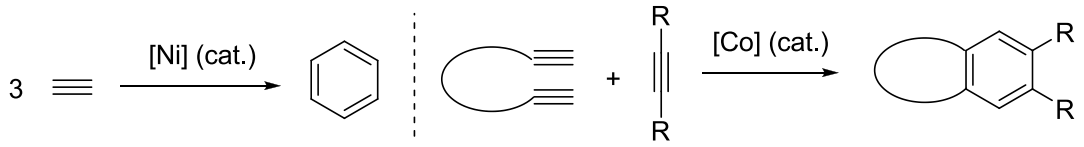
Iridium-Catalyzed Cyclodimerization of Diarylacetylenes giving Multisubstituted Naphthalenes

The $[IrCl(cod)]_2$/dppe/HCl system successfully catalyzes cyclodimerization of diarylacetylenes to give multisubstituted naphthalenes in high yields. Hydrogen chloride as an additive is effective to generate iridium-hydride species which is an active intermediate in the reaction.

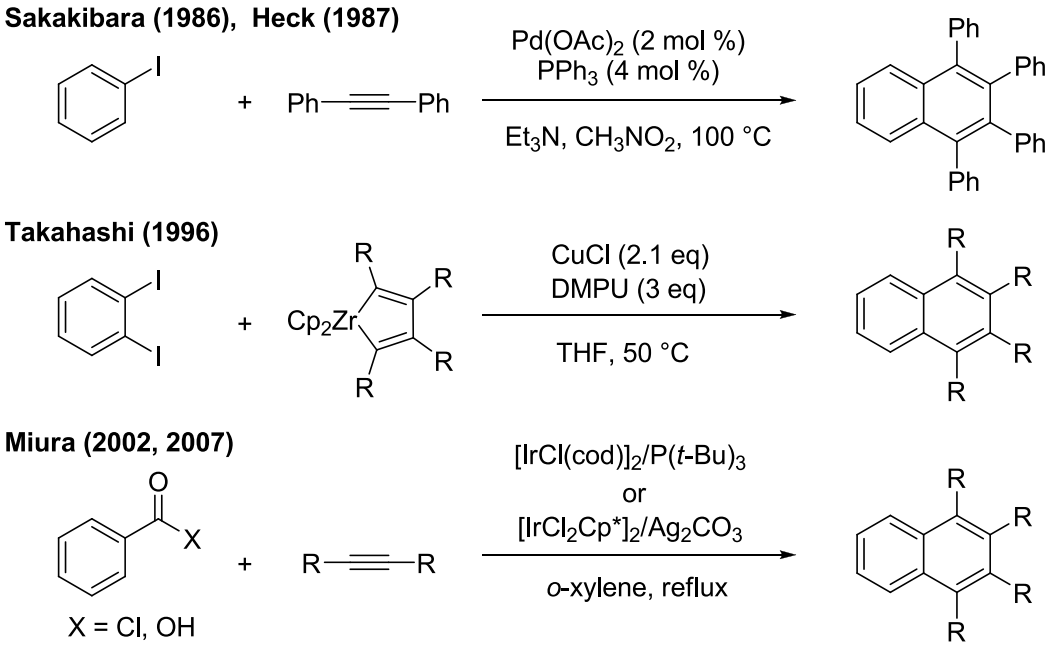


5-1. Introduction

Substituted polycyclic aromatic compounds have been of great significance in π-conjugated functional materials.[1] Since the discovery of Reppe's trimerization of acetylenes to produce benzenes,[2] the transition-metal-mediated oligomerization of alkynes is one of the most powerful synthetic tools for the construction of carbo- and heterocycles (Scheme 5-1).[3] Annulative condensation on benzene ring is also reliable strategy for synthesis of polycyclic aromatic hydrocarbons such as naphthalene and anthracene (Scheme 5-2). At early stages, Sakakibara and Heck independently reported palladium-catalyzed annulation of aryl halide with two equivalent amounts of alkynes to prepare naphthalene derivatives.[4] Takahashi developed the copper-mediated cycloaddition of *ortho*-dihalobenzene with zirconacyclopentadiene to construct fused arenes.[5] Formation of polycyclic aromatic compounds from benzoyl chlorides or benzoic acids and internal alkynes via decarbonylative or decarboxylative annulations was accomplished by Miura in the presence of iridium catalysts, respectively.[6]



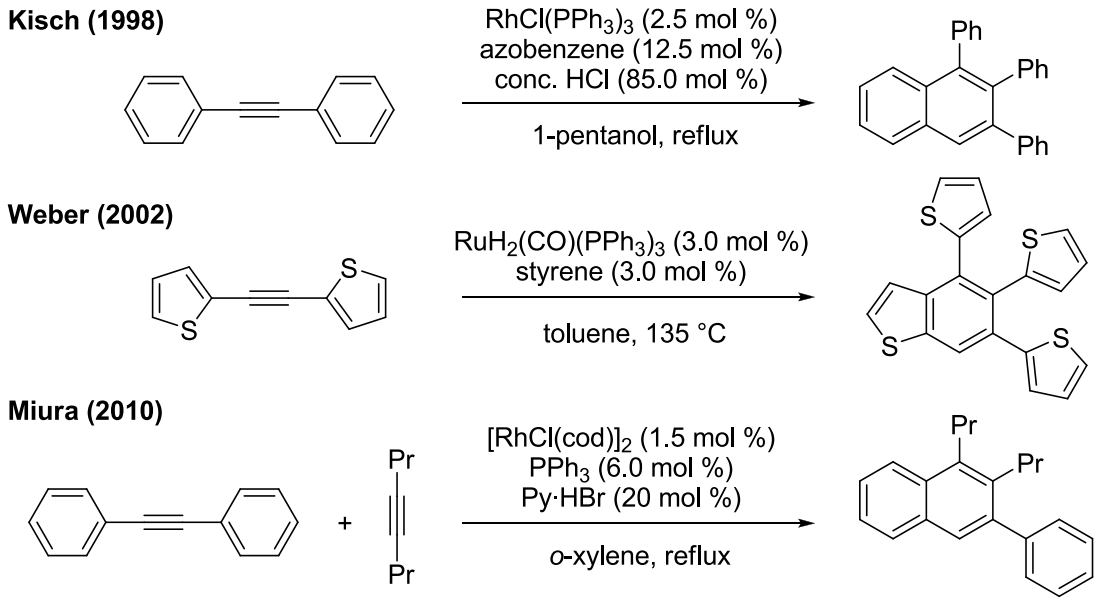
Scheme 5-1. [2+2+2] Cyclotrimerization of alkynes.



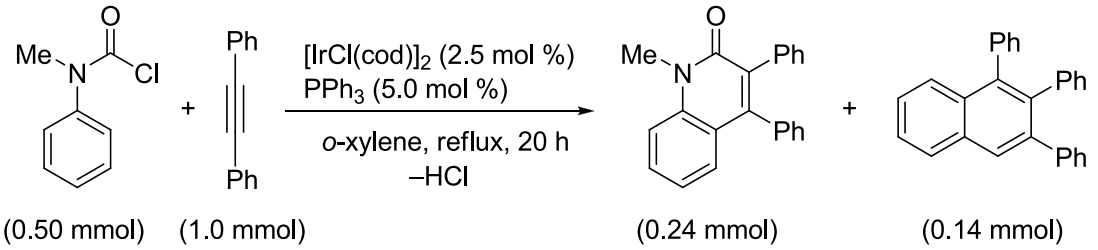
Scheme 5-2. Transition-metal-mediated annulative condensation on a phenyl ring.

In the view point of atom economy, cyclodimerization of diarylacetylenes is an attractive method for construction of multisubstituted naphthalenes. However, to date, there are only three examples to realize this strategy. In 1998, Kisch reported pioneering rhodium-catalyzed cyclodimerization of diarylacetylenes in the presence of conc. hydrochloric acid as an additive (Scheme 5-3).[7] Although it is an ideal waste-free protocol, the reaction conditions are quite restricted; 1) an excess amount of conc. HCl, 2) several additives to stabilize the catalyst, and 3) high boiling point alcohol as a solvent. After that, Weber described similar transformation catalyzed by the combination of $RuH_2(CO)(PPh_3)_3$ and styrene.[8] Recently, Miura successfully made the improvement of the rhodium catalyst system by using pyridine/HBr salt as an additive,[9] instead of conc. HCl. In addition of *homo*-cyclodimerization of diarylacetylenes, the catalysis could be applied to the chemoselective *cross*-cyclodimerization of aryl- and alkylalkynes.

In the Chapter 4, the author demonstrated the iridium-catalyzed annulations of *N*-arylcarbamoyl chlorides with internal alkynes to provide 2-quinolones. During the investigation, the author found that the reaction of *N*-methyl-*N*-phenylcarbamoyl chloride and diphenylacetylene afforded the corresponding 2-quinolone and 1,2,3-triphenylnaphthalene (Scheme 5-4). This result indicates that the naphthalene derivative would be generated via cyclodimerization of diphenylacetylene under the conditions. In this Chapter, the author describes a novel iridium-catalyzed cyclodimerization of diarylacetylenes to prepare multisubstituted naphthalenes in the presence of HCl as an additive.



Scheme 5-3. Transition-metal-catalyzed cyclodimerization of alkynes.



(0.50 mmol) (1.0 mmol) (0.24 mmol) (0.14 mmol)

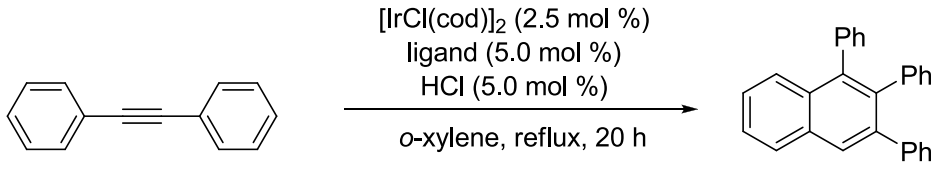
Scheme 5-4. The reaction of *N*-methyl-*N*-phenylcarbamoyl chloride and diphenylacetylene in the presence of the iridium catalyst.

5-2. Results and Discussion

Firstly the cyclodimerization of diphenylacetylene (**1a**) was carried out by employing various ligands in the presence of catalytic amount of $[IrCl(cod)]_2$ with anhydrous HCl as an additive (Table 5-1). As mentioned previously,[7,9] addition of HCl easily led to generate metal–hydride species *in situ*. Without any ligands, the cyclodimerization did not take place and most of **1a** was recovered (entry 1). When 5 mol % of PPh_3 (P/Ir =1) was used, desired product, 1,2,3-triphenylnaphthalene (**2a**), was obtained in 41% yield (entry 2). With 10 mol % of PPh_3 (P/Ir =2), the yield of **2a** increased to 95% yield. The structure of **2a** was unambiguously characterized by X-ray diffraction study. $P(4\text{-}MeOC_6H_4)_3$, $P(4\text{-}FC_6H_4)_3$ and $P(Mes)_3$ afforded **2a** in moderate to good yields (entries 3–5). Higher basicity ligands which are P(*n*-Bu)$_3$, PCy_3 and IPr were less effective (entries 6–8). Bidentate phosphines such as dppe, dppbz and dppp also gave better results to provide **2a** in high yields (entries 9–11). As increasing bite angle of bidentate phosphines, the yields decreased progressively (entries 12–15). In the case of dppm having smallest bite angle, **2a** was obtained in only 8% yield (entry 16).

Next, the effects of additives were examined under the combination of $[IrCl(cod)]_2$/dppe system in refluxing *o*-xylene (Table 5-2). In the absence of an additive, **2a** was obtained in 16% yield (entry 1). When 5 mol % of HCl in 4 M dioxane solution was used, **2a** was provided quantitatively (entry 2). Concentrated HCl aq. and HBr aq. were also effective in the reaction (entries 3 and 4). The use of *p*-$TsOH\cdot H_2O$ slightly decreased the yield of **2a** (entry 5). The catalytic activity dropped drastically when acetic acid and trifluoroacetic acid were used (entries 6 and 7). Acid chlorides were useful additives to generate metal-hydride species *in situ* via decarbonylation followed by *β*-hydride elimination.[10] Actually, octanoyl chloride as an additive afford **2a** in 60% yield (entry 8). The use of amine salts, which were good additives in Miura's rhodium catalyst system,[9] were also effective in the iridium catalyst system (entries 9–12) and notably $Et_3N\cdot HBr$ provides **2a** in 92% yield.

Table 5-1. Effect of ligands in the iridium-catalyzed cyclodimerization of diphenylacetylene (**1a**).[a]

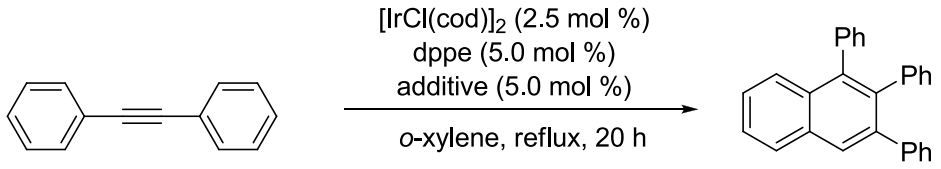


1a **2a**

entry	ligand	**2a** % yield[b]
1	none	3
2	PPh_3	41 (95)[c]
3	$P(4\text{-}MeOC_6H_4)_3$	44
4	$P(4\text{-}FC_6H_4)_3$	73
5	$P(Mes)_3$	74
6	$P(n\text{-}Bu)_3$	31
7	PCy_3	29
8	IPr	2[d]
9	dppe (85 °)[e]	99 (81)[f]
10	dppbz (83 °)[e]	95
11	dppp (91 °)[e]	87
12	dppb (98 °)[e]	51
13	dppf (99 °)[e]	29
14	binap (93 °)[e]	12
15	xantphos (111°)[e]	3
16	dppm (72 °)[e]	8

[a] Conditions; diphenylacetylene (**1a**) (0.5 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), ligand (0.025 mmol, 5.0 mol %), HCl (4 M in dioxane, 5.0 mol %) in refluxing *o*-xylene (1.0 mL), for 20 h. [b] Determined by GC analysis. [c] Using 10 mol % of PPh_3 (P/Ir = 2). [d] Using 5.0 mol % of IrCl(cod)(IPr) instead of $[IrCl(cod)]_2$. [e] Natural bite angle. [f] Isolated yield.

Table 5-2. Effect of additives in the iridium-catalyzed cyclodimerization of diphenylacetylene (**1a**).[a]



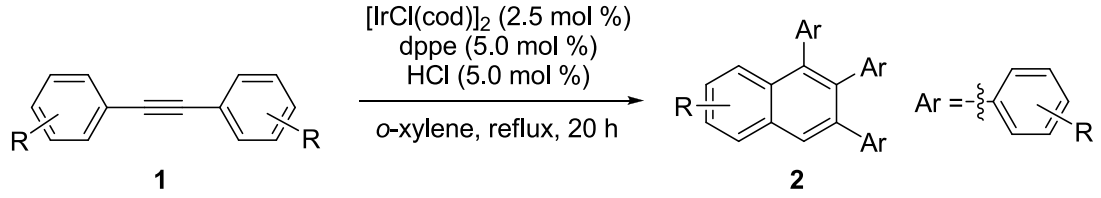
1a **2a**

entry	additive	**2a** % yield[b]
1	none	16
2	HCl (4 M in dioxane)	99
3	conc. HCl aq.	95
4	conc. HBr aq.	85
5	*p*-TsOH·H_2O	64
6	CH_3COOH	18
7	CF_3COOH	16
8	*n*-$C_7H_{15}COCl$	60
9	Py·HCl	35
10	Py·HBr	52
11	Et_3N·HCl	85
12	Et_3N·HBr	92

[a] Conditions; diphenylacetylene (**1a**) (0.5 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), dppe (0.025 mmol, 5.0 mol %), additive (5.0 mol %) in refluxing *o*-xylene (1.0 mL), for 20 h. [b] Yields were determined by GC analysis.

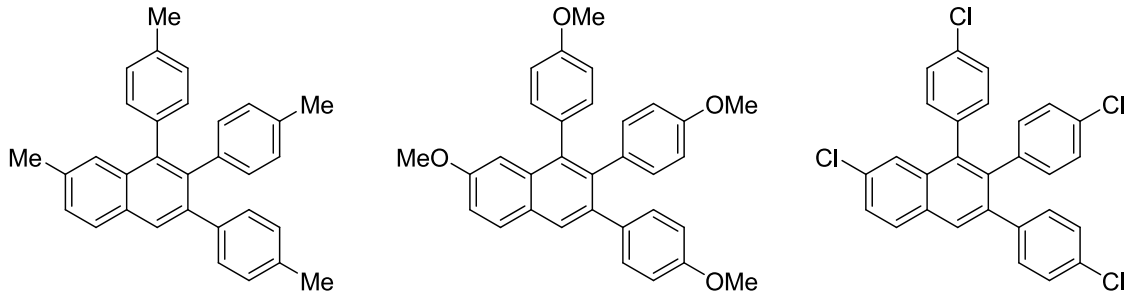
The cyclodimerization of various diarylacetylenes was carried out in the $[IrCl(cod)]_2$/deep system with anhydrous HCl as an additive (Table 5-3). Both electron-rich and electron-poor substituted diarylacetylenes **1b**–**g** successfully gave multisubstituted naphthalenes **2b**–**g** in good to high yields. It was noteworthy that cyclodimerizations of *meta*-substituted diarylacetylenes such as **1f** and **1g** regioselectively afforded **2f** and **2g**, respectively, as single isomers. However, *ortho*-substituted diarylacetylenes was unsuccessful probably due to the steric hindrance. Unfortunately, aryl-alkylacetylene such as 1-phenyl-1-propyne could not be applied to the reaction because the insertion of the second alkyne to an iridium-hydride species may be inhibited by the diminished reactivity of the intermediate (*vide infra*).

Table 5-3. Iridium-catalyzed cyclodimerization of diarylacetylenes **1**.[a,b]

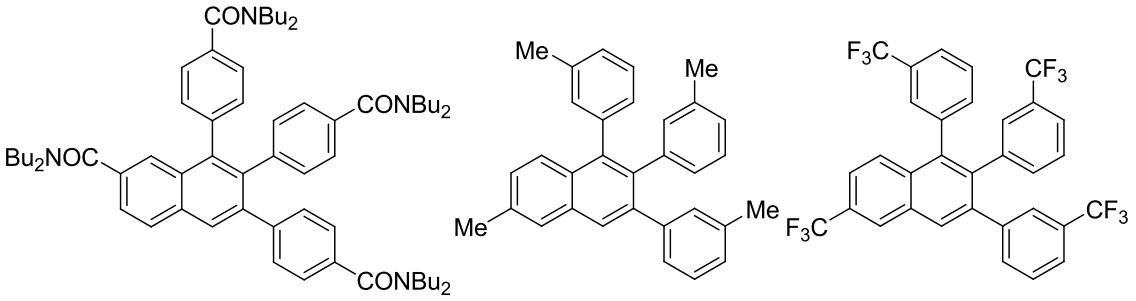


1 **2**

1b: R = 4-Me, **1c**: R = 4-MeO, **1d**: R = 4-Cl, **1e**: R = 4-Bu_2NCO, **1f**: R = 3-Me, **1g**: R = 3-CF_3



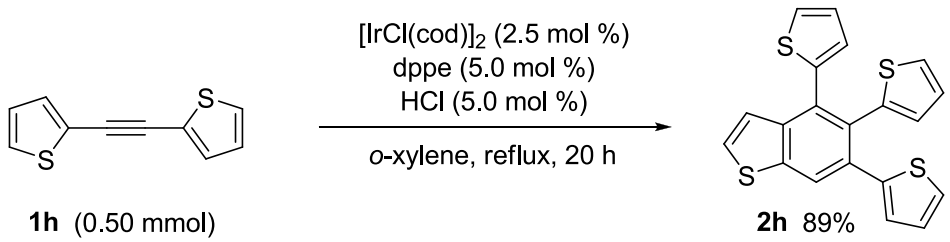
2b 80% **2c** 81% **2d** 76%[c]



2e 89% **2f** 93% **2g** 60%

[a] Conditions; diarylacetylene (**1**) (0.5 mmol), $[IrCl(cod)]_2$ (0.0125 mmol, 2.5 mol %), dppe (0.025 mmol, 5.0 mol %), HCl (4 M in dioxane, 5.0 mol %) in refluxing *o*-xylene (1.0 mL), for 20 h. [b] Isolated yields. [c] *o*-xylene (2 mL).

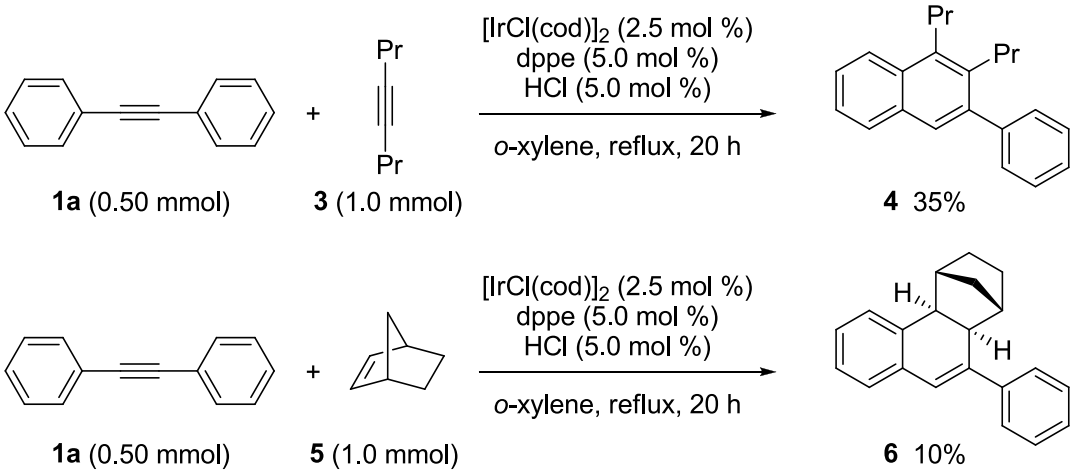
The present iridium-catalyzed system could be participated in the diheteroarylacetylene as a substrate. For example, dithienylacetylene (**1h**) afforded the corresponding benzothiophene **2h** in 89% yield (Scheme 5-5).



1h (0.50 mmol) **2h** 89%

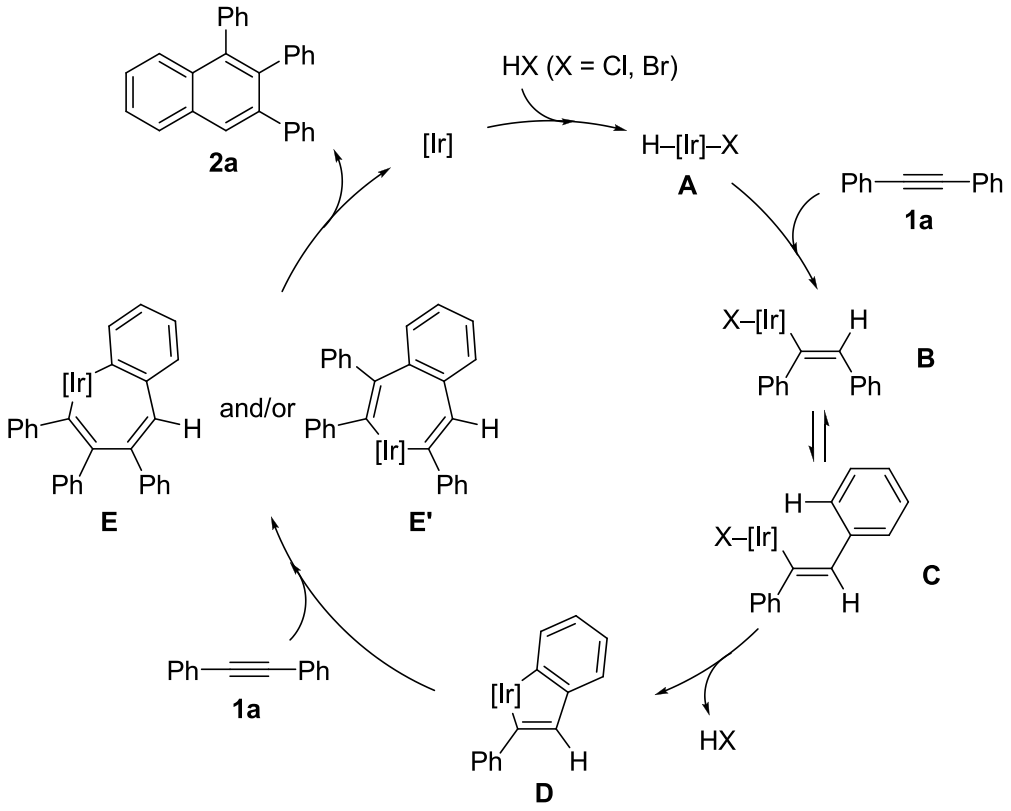
Scheme 5-5. Iridium-catalyzed cyclodimerization of **1h**.

Next, the author tried to apply the catalyst to the *cross*-dimerization of diarylacetylenes with dialkylacetylenes or alkenes (Scheme 5-6).[9] As the preliminary results, the reaction of **1a** with 4-octyne (**3**) afforded cross-dimerization product **4** in 35% yield determined by GC analysis, albeit quite amount of **2a** was also generated. In the case of norbornene (**5**), **6** was obtained in only 10% yield. When Et_3N·HBr or Py·HBr as an additive was used instead of anhydrous HCl,[9] the yields of desired cross-dimerization products were not improved.

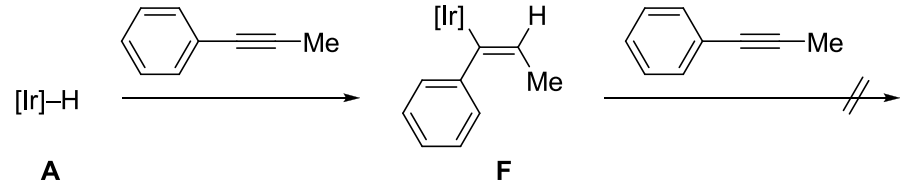


Scheme 5-6. Iridium-catalyzed cross-dimerization of **1a** with 4-octyne or norbornene.

A plausible reaction mechanism of cyclodimerization is shown in Scheme 5-7. First, addition of HX (X = Cl, Br) to the iridium(I) precursor gives iridium-hydride(III) species **A**.[11] The subsequent insertion of diarylacetylene **1a** into the iridium–hydride bond followed by isomerization via a zwitterionic form would afford the intermediate **C**.[12] *ortho*-Metalation from the iridium complex **C** may occur to generate a five-membered iridacycle complex **D** with the elimination of HX.[7–9] Second **1a** would insert to the iridium–alkenyl or –aryl bond on **D** to afford a seven-membered iridacycle complex **E** or **E'**, respectively. Finally, reductive elimination could produce the desired cyclodimerization product **2a** and regenerate the active iridium species. In the case of *cross*-dimerization of diarylacetylenes with alkynes or alkenes, second carbon-carbon unsaturated molecules would insert to the intermediate **D** affording the desired products, albeit *homo*-dimerization of diarylacetylenes is also competed under the iridium-catalyzed system. When the aryl-alkylacetylenes were used as a substrate, the insertion of alkynes would occur to generate a vinyl-iridium species **F** sided on the aryl group (Scheme 5-8). The putative intermediate **F** might diminish the reactivity toward the insertion of the second alkyne.



Scheme 5-7. Plausible reaction mechanism.



Scheme 5-8. Insertion of aryl-alkylacetylenes to the iridium-hydride species **A**.

5-3. Conclusion

In summary, multisubstituted naphthalenes **2** have been successfully obtained by an iridium-catalyzed cyclodimerization of diarylacetylenes **1**. It was essential for hydrogen chloride as an additive to generate the active iridium–hydride species *in situ* for the reaction.

5-4. Experimental Section

Instrumentation and chemicals

All manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. All solvents were dried and purified by usual procedures.[13] Unless otherwise noted, materials obtained from

commercial suppliers were used without further purification. $[IrCl(cod)]_2$ was prepared according to the literature.[14] Diphenylacetylene **1a** was purchase from Wako. Diarylacetylenes **1b–h** were prepared according to the literatures.[15] IR spectra were obtained on a SHIMADZU FTIR-8300 spectrometer. ^1H and ^{13}C NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^1H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). EI-MS were recorded on a Shimadzu GCMS-QP5050A with a direct inlet. High-resolution mass spectra (ESI-HRMS) were obtained with a JEOL SX-102A spectrometer. GC analysis was carried out using a Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$.

General procedure in Table 5-1

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and a ligand (0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. Anhydrous HCl in dioxane (4 M, 6.5 μL, 0.026 mmol) was added to the flask and the mixture was stirred further for 10 min at room temperature. Subsequently, **1a** (89.1 mg, 0.50 mmol) was added to the flask and the mixture was heated under reflux (bath temp. 155 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with dichloromethane (5.0 mL) and added tridecane (50 μL, 0.205 mmol) as an internal standard. The yield of the product **2a** was determined by GC analysis.

General procedure in Table 5-2

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and dppe (10.0 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. An additive (0.025 mmol) was added to the flask and the mixture was stirred further for 10 min at room temperature. Subsequently, **1a** (89.1 mg, 0.50 mmol) was added to the flask and the mixture was heated under reflux (bath temp. 155 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted

with dichloromethane (5.0 mL) and added tridecane (50 μL, 0.205 mmol) as an internal standard. The yield of the products **2a** was determined by GC analysis.

General procedure in Table 5-3

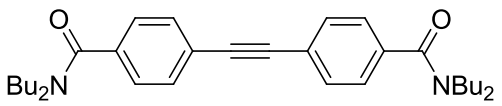
$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and dppe (10.0 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. Anhydrous HCl in dioxane (4 M, 6.5 μL, 0.026 mmol) was added to the flask and the mixture was stirred further for 10 min at room temperature. Subsequently, diarylacetylene **1** (0.50 mmol) was added to the flask and the mixture was heated under reflux (bath temp. 155 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the mixture was evaporated and the product was isolated by silica gel column chromatography using CH_2Cl_2–hexane followed by GPC.

Procedures for cross-dimerization of 1a with alkyne or alkene in Scheme 5-6

$[IrCl(cod)]_2$ (8.4 mg, 0.0125 mmol) and dppe (10.0 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a reflux condenser and a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then *o*-xylene (1.0 mL) was added to the flask and the resultant solution was stirred at room temperature for 10 min. Subsequently, anhydrous HCl in dioxane (4 M, 6.5 μL, 0.026 mmol) was added to the flask and the mixture was stirred further for 10 min at room temperature. **1a** (89.1 mg, 0.50 mmol) and 4-octyne (135 μL, 1.0 mmol), or norbornene (94.1 mg, 1.0 mmol), was added to the flask and the mixture was heated under reflux (bath temp. 155 °C) for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with dichloromethane (5.0 mL) and added tridecane (50 μL, 0.205 mmol) as an internal standard. The yields of the products (**4** and **6**) were determined by GC analysis, compared to authentic samples.[9]

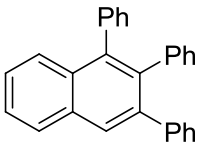
Characterization of the Compounds

Bis(4-*N*,*N*-dibutylamidephenyl)acetylene (**1e**)[16]



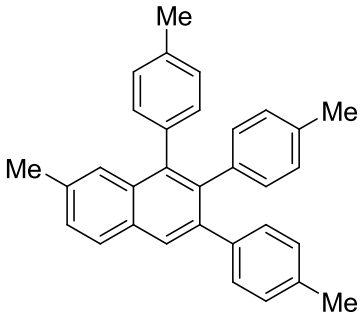
Pale brown solids. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.9 Hz, 4H), 7.35 (d, J = 7.9 Hz, 4H), 3.49 (brd, 4H), 3.19 (brd, 4H), 1.64 (brd, 4H), 1.49 (brd, 4H), 1.41 (brd, 4H), 1.14 (brd, 4H), 0.98 (brd, 6H), 0.80 (brd, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.9, 137.2, 131.6, 126.6, 123.7, 89.8, 48.8, 44.5, 30.8, 29.6, 20.3, 19.7, 13.9, 13.6.

1,2,3-Triphenylnaphthalene (**2a**)[9]



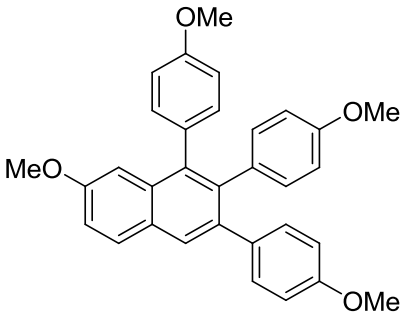
White solids, 144 mg, 81% yield. Identified by ^{1}H NMR spectrum according to the reported data: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.93 (d, J = 7.4 Hz, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.51 (t, J = 7.0 Hz, 1H), 7.38 (t, J = 7.4 Hz, 1H), 7.28-7.14 (m, 10H), 6.95-6.91 (m, 3H), 6.87-6.84 (m, 2H).

7-Methyl-1,2,3-tris(4-methylphenyl)naphthalene (**2b**)[9]



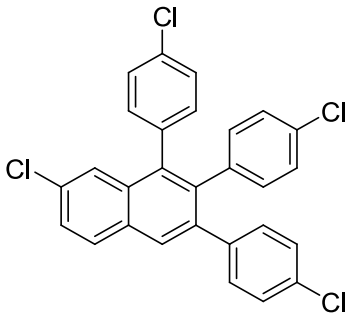
White solids, 168 mg, 80% yield. Identified by ^{1}H NMR spectrum according to the reported data: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.30 (s, 1H), 7.06-6.95 (m, 9H), 6.73 (m, 4H), 2.39 (s, 3H), 2.33 (s, 3H), 2.28 (s, 3H), 2.16 (s, 3H).

7-Methoxy-1,2,3-tris(4-methoxyphenyl)naphthalene (**2c**)[9]



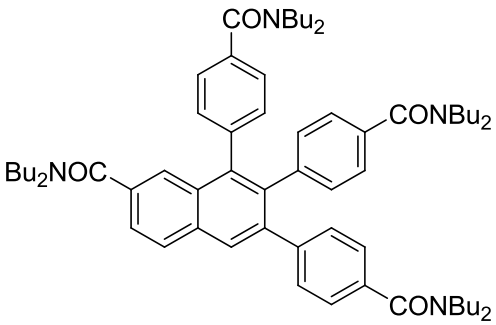
Pale yellow solids, 193 mg, 81% yield. Identified by ^{1}H NMR spectrum according to the reported data: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.14 (dd, J = 12.0, 2.2 Hz, 1H), 7.06-7.01 (m, 4H), 6.88 (s, 1H), 6.78 (dt, J = 8.8, 2.2 Hz, 2H), 6.74 (dt, J = 8.8, 2.2 Hz, 2H), 6.71 (dt, J = 8.8, 2.2 Hz, 2H), 6.51 (dt, J = 8.8, 2.2 Hz, 2H), 3.77 (s, 3H), 3.71 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H).

7-Chloro-1,2,3-tris(4-chlorophenyl)naphthalene (**2d**)[9]



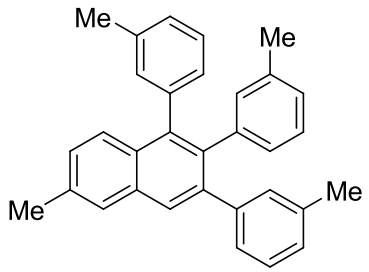
White solids, 188 mg, 76% yield. Identified by ^{1}H NMR spectrum according to the reported data: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.48-7.44 (m, 2H), 7.25 (dt, J = 8.4, 2.6 Hz, 2H), 7.17 (dt, J = 8.4, 2.6 Hz, 2H), 7.07-7.02 (m, 4H), 6.97 (dt, J = 8.4, 2.6 Hz, 2H), 6.74 (dt, J = 8.4, 2.6 Hz, 2H).

7-*N*,*N*-Dibutylamide-1,2,3-tris(4-*N*,*N*-dibutylamidephenyl)naphthalene (**2e**)



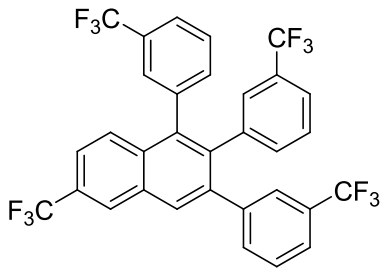
Pale yellow amorphous, 216 mg, 89% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 8.6 Hz, 1H), 7.99 (s, 1H), 7.56 (s, 1H), 7.53 (dd, J = 8.2, 1.4 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.22-7.15 (m, 6H), 6.97 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 3.54-3.34 (m, 8H), 3.22-2.97 (m, 8H), 1.69-1.25 (m, 24H), 1.23-1.02 (m, 8H), 1.02-0.69 (m, 24H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.95, 170.93, 170.84, 170.68, 141.84, 140.13, 139.23, 139.20, 138.68, 137.34, 135.56, 135.26, 135.24, 134.65, 132.37, 131.08, 130.81, 130.78, 129.61, 128.92, 128.29, 125.92, 125.77, 125.30, 124.63, 123.80, 48.43 (br), 44.08 (br), 30.43 (br), 29.28 (br), 19.95 (br), 19.48 (br), 13.81 (br). IR (neat): 2929.7, 2871.8, 1633.6, 1423.4, 1296.1, 1099.3 cm^{-1}. ESI-HRMS: Calcd. for $C_{64}H_{89}N_4O_4$ ([M+H]$^+$), 977.6878. Found, 977.6874.

6-Methyl-1,2,3-tris(3-methylphenyl)naphthalene (**2f**)



Pale yellow amorphous, 192 mg, 93% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.65 (s, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.18 (d, J = 8.6 Hz, 1H), 7.10-6.87 (m, 8H), 6.79 (t, J = 7.3 Hz, 1H), 6.71-6.61 (m, 3H), 2.48 (s, 3H), 2.28-2.18 (m, 6H), 2.02 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.13, 140.00, 139.97, 139.50, 138.98, 137.30, 136.80, 136.72, 136.62, 135.86, 135.46, 132.83, 132.45, 132.01, 131.94, 130.82, 130.25, 128.59, 128.33, 128.19, 127.81, 127.19, 127.13, 126.93, 126.82, 126.78, 126.48, 126.06, 21.52, 21.32, 21.32, 21.11. IR (neat): 3026.1, 2920.0, 1604.7, 783.0, 707.8 cm^{-1}. ESI-HRMS: Calcd. for $C_{32}H_{29}$ ([M+H]$^+$), 413.2264. Found, 413.2265.

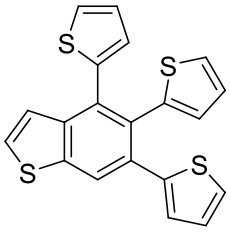
6-Trifluoromethyl-1,2,3-tris(3-trifluoromethylphenyl)naphthalene (**2g**)



Pale yellow amorphous, 95.0 mg, 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 8.12 (s, 1H), 7.70-7.63 (m, 2H), 7.54-7.32 (m, 7H), 7.27 (t, J = 8.2 Hz, 2H), 7.17-7.06 (m, 2H), 7.03-6.95 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.08, 141.05, 139.43, 139.39, 139.35, 139.32, 138.90, 138.84, 138.76, 138.72, 138.42, 138.36, 134.27, 133.97, 133.00, 131.84, 131.81, 130.92, 130.61, 130.29, 130.16, 130.12, 129.02, 128.69, 128.52, 128.07, 128.01, 127.72, 126.78 (q, J = 4.8 Hz), 125.94

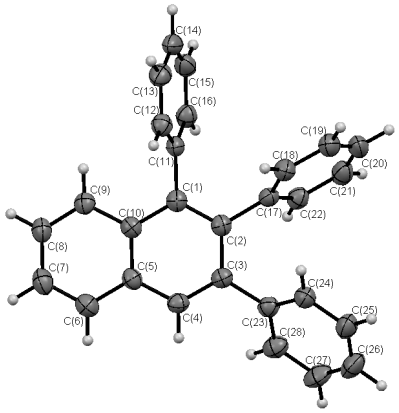
(q, J = 3.8 Hz), 125.49, 125.16, 124.20, 123.82 (q, J = 3.8 Hz), 123.33, 122.77 (q, J = 2.9 Hz), 122.42. The ^{13}C NMR spectrum was very complex due to C-F coupling. All signals observed were shown. IR (neat): 1326.9, 1166.9, 1124.4, 1074.3 cm^{-1}. ESI-HRMS: Calcd. for $C_{32}H_{16}F_{12}$ ([M]$^+$), 628.1055. Found, 628.1064.

4,5,6-Tri(2-thienyl)benzo[*b*]thiophene (**2h**)[9]



Brown solids, 169 mg, 89% yield. Identified by ^{1}H NMR spectrum according to the reported data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.44 (d, J = 5.8 Hz, 1H), 7.29 (dd, J = 4.4, 1.8 Hz, 1H), 7.25 (d, J = 6.2 Hz, 1H), 7.22-7.18 (m, 2H), 6.99-6.96 (m, 2H), 6.91 (t, J = 4.4, 1H), 6.87 (d, J = 3.7 Hz, 1H), 6.81 (t, J = 4.4, 1H), 6.71 (d, J = 3.7 Hz, 1H).

X-ray Diffraction Study of 2a



Single crystal of **2a** was obtained by recrystallization from hot hexane solution. Crystal data for **2a**: $C_{28}H_{20}$, M = 356.47, monoclinic, space group = $P2_1/a$ (#14), a = 9.384(3) Å, b = 21.490(8) Å, c = 10.054(4) Å, β = 106.562(4)°, V = 1943.4(12) Å^3, Z = 4, density (calc.) = 1.218, total reflections collected = 14394, unique reflections = 4373 (R_{int} = 0.080), GOF = 1.002. The final $R1$ factor was 0.0538 ($I>2\sigma(I)$) ($wR2$ = 0.1099, all data).

5-5. References and Notes

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List of Publications

I. The present Thesis is composed of the following papers.

Chapter 1

(1) The iridium-catalyzed decarbonylation of aldehydes under mild conditions
Tomohiro Iwai, Tetsuaki Fujihara, Yasushi Tsuji
Chem. Commun. **2008**, 6215–6217.

Chapter 2

(2) Iridium-Catalyzed Addition of Acid Chlorides to Terminal Alkynes
Tomohiro Iwai, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
J. Am. Chem. Soc. **2009**, *131*, 6668–6669.

Chapter 3

(3) Iridium-Catalyzed Addition of Aliphatic Acid Chlorides to Terminal Alkynes without Decarbonylation
Tomohiro Iwai, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
In preparation.

Chapter 4

(4) Iridium-Catalyzed Annulation of *N*-Arylcarbamoyl Chlorides with Internal Alkynes
Tomohiro Iwai, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
J. Am. Chem. Soc. **2010**, *132*, 9602–9603.

Chapter 5

(5) Iridium-Catalyzed Cyclodimerization of Diarylacetylenes giving Multisubstituted Naphthalenes
Tomohiro Iwai, Tomoya Hosoki, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
In preparation.

II. Following publications are not included in this Thesis.

(6) Palladium-Catalyzed Hydroesterification of Alkynes Employing Aryl Formates without the Use of External Carbon Monoxide
Yuko Katafuchi, Tetsuaki Fujihara, Tomohiro Iwai, Jun Terao, Yasushi Tsuji
Adv. Synth. Catal. **2011**, in press.

(7) Palladium-Catalyzed Intermolecular Addition of Formamides to Alkynes
Tetsuaki Fujihara, Yuko Katafuchi, Tomohiro Iwai, Jun Terao, Yasushi Tsuji
J. Am. Chem. Soc. **2010**, *132*, 2094–2098.

(8) Multi-Input/Multi-Output Molecular Response System Based on the Dynamic Redox Behavior of 3,3,4,4-Tetraaryldihydro[5]helicene Derivatives: Reversible Formation/Destruction of Chiral Fluorophore and Modulation of Chiroptical Properties by Solvent Polarity
Takanori Suzuki, Yusuke Ishigaki, Tomohiro Iwai, Hidetoshi Kawai, Kenshu Fujiwara, Hitoshi Ikeda, Yusuke Kano, Kazuhiko Mizuno
Chem. Eur. J. **2009**, *15*, 9434–9441.

(9) Electrochiroptical systems based on biphenyl-2,2'-diyl-type dicationic dyes: Strong chiroptical signals through the transmission of point chirality to axial chirality
Takanori Suzuki, Tomohiro Iwai, Eisuke Ohta, Hidetoshi Kawai, Kenshu Fujiwara
Tetrahedron Lett. **2007**, *48*, 3599–3603.

(10) A Bowl-Shaped Phosphine as a Ligand in Palladium-Catalyzed Suzuki-Miyaura Coupling of Aryl Chlorides: Effect of a Depth of the Bowl
Hidetoshi Ohta, Makoto Tokunaga, Yasushi Obora, Tomohiro Iwai, Tetsuo Iwasawa, Tetsuaki Fujihara, Yasushi Tsuji
Org. Lett. **2007**, *9*, 89–92.

[Review]

(1) Transition-Metal-Catalyzed Additions of Carbonyl Functionalities to Alkynes
Tetsuaki Fujihara, Tomohiro Iwai, Jun Terao, Yasushi Tsuji
Synlett **2010**, 2537–2548.

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Tomohiro Iwai