

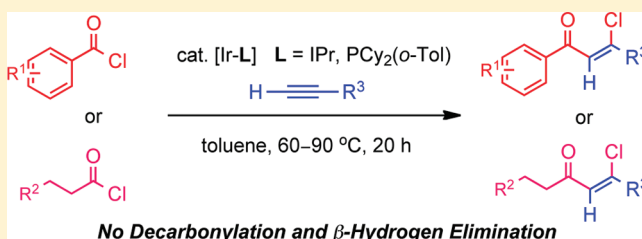
Iridium-Catalyzed Addition of Aroyl Chlorides and Aliphatic Acid Chlorides to Terminal Alkynes

Tomohiro Iwai,[†] Tetsuaki Fujihara, Jun Terao, and Yasushi Tsuji*

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Nishikyō-ku, Kyoto 615-8510, Japan

Supporting Information

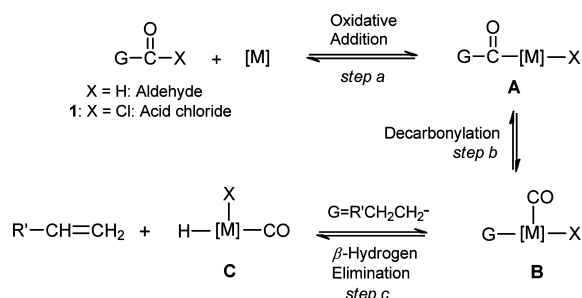
ABSTRACT: Iridium complexes show high catalytic activity in intermolecular additions of acid chlorides to terminal alkynes to afford valuable (*Z*)- β -chloro- α,β -unsaturated ketones. Ligands in the catalytic system play a crucial role in this reaction. An *N*-heterocyclic carbene (NHC) is an efficient ligand for the addition of aroyl chlorides, while dicyclohexyl(2-methylphenyl)phosphine (PCy₂(*o*-Tol)) is indispensable for the reaction of aliphatic acid chlorides. The addition reactions proceed regio- and stereoselectively with suppression of decarbonylation and β -hydrogen elimination, which have been two major intrinsic problems in transition-metal-catalyzed reactions. Stoichiometric reactions of active iridium catalysts with aroyl chlorides and aliphatic acid chlorides are carried out to gain insights into the reaction mechanisms.



INTRODUCTION

Highly atom-efficient¹ additions of carbonyl functionalities to carbon–carbon multiple bonds are extremely promising in realizing valuable and environmentally benign organic transformations.² In these addition reactions, the most common carbonyl sources are aldehydes (hydroacylation).³ Oxidative addition of aldehydes to different metal centers ($X = H$, step a in Scheme 1) has been reported.⁴ However, after oxidative

Scheme 1. Reaction of Aldehydes and Acid Chlorides with a Catalyst Center



addition, the carbonyl functionality is often lost via decarbonylation⁵ from the resulting acyl metal species A (step b). Therefore, catalytic additions of aldehydes to unsaturated compounds often suffer from low selectivity and low yields. To suppress such undesirable decarbonylation reactions, (1) intramolecular addition,⁶ (2) carbon monoxide pressure,⁷ and/or (3) substrates having proper directing groups⁸ have often been indispensable.^{9,10} In addition, when aliphatic aldehydes (such as $G = R'CH_2-CH_2$ in Scheme 1) are used

in the reactions, facile β -hydrogen elimination¹¹ from species B inevitably occurs to afford hydride species C (step c). Hence, the reactions often become more unselective.

On the other hand, oxidative addition of acid chlorides to a metal center is a facile step.¹² Thus, acid chlorides are promising substrates in the addition reaction.¹³ The addition to alkynes is particularly useful, as both carbonyl and chloro functionalities can be introduced atom-economically and simultaneously to afford valuable β -chloro- α,β -unsaturated ketones.¹⁴ In a transition-metal-catalyzed reaction, Miura and co-workers reported a pioneering rhodium-catalyzed addition of aroyl chlorides to terminal alkynes.^{13a} However, in their case, carbonyl functionality was completely lost by the facile decarbonylation reaction from the product during the reaction. Tanaka and co-workers found that in the presence of a rhodium catalyst, perfluorinated acid chlorides,^{15a} chloroacetyl chlorides,^{15b} and α -keto acid chlorides^{15c} successfully added to terminal alkynes without the decarbonylation. However, to prevent decarbonylation, the substrates were limited to these acid chlorides.¹⁶ Friedel–Crafts-type additions of acid chlorides to alkynes using a stoichiometric or catalytic amount of a Lewis acid are known.¹⁷ However, these reactions often suffer from the narrow scope of applicable substrates and/or low stereoselectivity of products.

Here, we report that an iridium complex bearing a suitable ligand successfully catalyzes the addition of acid chlorides to terminal alkynes, giving (*Z*)- β -chloro- α,β -unsaturated ketones regio- and stereoselectively. Importantly, both aroyl chlorides¹⁸ and aliphatic acid chlorides can be utilized in the addition

Received: October 14, 2011

Published: December 13, 2011

reaction with suppression of decarbonylation and β -hydrogen elimination, which have been two major intrinsic problems in transition-metal-catalyzed reactions.¹⁹ The key to the success of such a wide substrate applicability in the present iridium-catalyzed reaction is the appropriate choice of ligands depending on the substrates.

RESULT AND DISCUSSION

First, the addition of aroyl chlorides was examined,¹⁸ because aryl-metal species (**B**: with $G = \text{Ar}$, Scheme 1) generated by decarbonylation do not undergo β -hydrogen elimination. In Table 1, the reaction of benzoyl chloride (**1a**) with phenylacetylene

Table 1. Effect of Ligands on the Addition of Benzoyl Chloride (1a**) to Phenylacetylene (**2a**)^a**

entry	ligand	3aa % yield ^b (Z/E) ^c	4aa % yield ^b	
1	PPh ₃	6	<1	
2	PCy ₃	53 (94/6)	12	
3	PCy ₂ (<i>o</i> -Tol)	37 (88/12)	9	
4	PCy ₂ (<i>o</i> -biphenyl)	20 (89/11)	4	
5	XPhos	46 (91/9)	28	
6	IMes·HCl/ <i>t</i> -BuOK	37 (87/13)	4	
7	IPr·HCl/ <i>t</i> -BuOK	88 (98/2)	2	
8	[IrCl(cod)(IPr)] ^d	(91) ^e (99/1)	<1	
9	SPhos	12	61	
10	RuPhos	9	72 (70) ^e	

^aConditions: Benzoyl chloride (**1a**, 0.50 mmol), phenylacetylene (**2a**, 0.75 mmol), [IrCl(cod)]₂ (0.0125 mmol, 2.5 mol %), added ligand (0.025 mmol, 5.0 mol %), toluene (1.0 mL), under reflux, for 20 h.

^bYield based on the GC internal standard technique by using tridecane as an internal standard. ^cZ/E ratio was determined by GC analysis.

^d[IrCl(cod)(IPr)] (0.025 mmol, 5.0 mol %) was used as the catalyst at 90 °C. ^eYield of isolated product.

(**2a**) was carried out employing various ligands with a catalytic amount of [IrCl(cod)]₂. Using PPh₃ as a ligand, the desired adduct (**3aa**) was afforded only in 6% yield in refluxing toluene (entry 1). Tricyclohexylphosphine (PCy₃; Cy = cyclohexyl) afforded **3aa** in moderate (53%) yield, but with a considerable amount (12%) of the decarbonylated product (**4aa**) (entry 2). Other phosphine ligands such as PCy₂(*o*-Tol),²⁰ PCy₂(*o*-biphenyl), and XPhos²¹ (Figure 1) gave

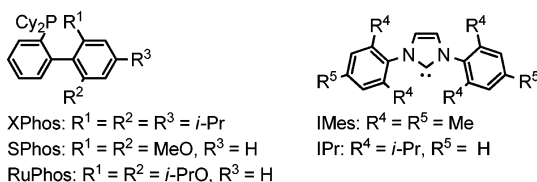


Figure 1. Structures of ligands.

mixtures of **3aa** and **4aa** in low yields (entries 3–5). As for NHC ligands, IMes generated in situ from IMes·HCl and *t*-BuOK provided **3aa** and **4aa** in 37% and 4% yields, respectively (entry 6). Gratifyingly, IPr generated from IPr·HCl and *t*-BuOK is much more effective to afford **3aa** selectively in 88% yield (entry 7). By the use of an isolated iridium–NHC complex, [IrCl(cod)(IPr)]²² **3aa** was obtained more effectively

with high (Z)-selectivity even at 90 °C (91% yield, Z/E = 99/1; entry 8). In contrast, with phosphines such as SPhos²¹ and RuPhos²¹ (Figure 1), the decarbonylated product **4aa** was obtained fairly selectively as a major product in 61% and 72% yields, respectively (entries 9 and 10). Thus, the ligand in the catalytic system played a critical role in determining the selectivity of the products. As for solvents, in dioxane the product **3aa** was afforded in 86% yield, whereas the reaction did not proceed in propionitrile and *N,N*-dimethylformamide under conditions identical to those of entry 8.

As reported preliminarily,¹⁸ the corresponding β -chloro- α , β -unsaturated aromatic ketones (**3**) were obtained regio- and (Z)-stereoselectively from various aroyl chlorides and terminal alkynes. Representative examples were shown in Table 2.

Table 2. Addition of Aroyl Chlorides (1**) to Terminal Alkynes (**2**) without Decarbonylation^a**

entry	1	2	3
1			
			3ba : 91% ^{b,c}
2			
			3ca : 92% ^{b,c}
3			
			3ab : 88% ^{b,c}

^aConditions: Aroyl chlorides (**1**, 0.50 mmol), alkynes (**2**, 0.75 mmol), [IrCl(cod)(IPr)] (0.025 mmol, 5.0 mol %), toluene (1.0 mL), at 90 °C, for 20 h. ^bIsolated yields. ^cZ/E > 99/1.

Electron-rich (**1b**) and electron-poor aroyl chlorides (**1c**) reacted smoothly with **2a** without decarbonylation to give **3ba** and **3ca** in high yields (entries 1 and 2). An aliphatic terminal alkyne (**2b**) also provided the adduct **3ab** (entry 3).

For aliphatic acid chlorides, the most active catalyst for aroyl chlorides, [IrCl(cod)(IPr)] (Table 2), was not effective. With this [IrCl(cod)(IPr)] as a catalyst, the reaction of stearoyl chloride (**1d**) with **2b** afforded the desired product (**3db**) in only 29% isolated yield (entry 1, Table 3). Combinations of the Ir precursor [IrCl(cod)]₂ and a wide variety of ligands induced little or no catalytic activity (entries 2–8). In these cases, a considerable amount of 1-heptadecene (**5**) was formed via decarbonylation followed by facile β -hydrogen elimination. Like aroyl chlorides, phenylacetyl chloride (**1e**) does not undergo β -hydrogen elimination after the decarbonylation. However, even for **1e**, [IrCl(cod)(IPr)] was not an active catalyst (entry 10). The [IrCl(cod)]₂/RuPhos catalyst system also gave a complex mixture (entry 11). Among the ligands examined, PCy₂(*o*-Tol)²⁰ is a very unique ligand and brought about a highly active catalyst system for both **1d** and **1e** to afford the adducts (**3db** and **3eb**) in high yields without decarbonylation and β -hydrogen elimination (entries 9 and 12). As mentioned above, the use of other ligands with similar steric and/or electric natures such as PCy₃, PCy₂Ph, PCy₂(*o*-biphenyl), XPhos, and RuPhos resulted in lower yields of **3db** (entries 4–8). In dioxane and 1,2-dichloroethane, the product **3db** was obtained in 84% and 72% yields, respectively, while the reaction did not proceed in *N,N*-dimethylacetamide and acetonitrile under conditions identical to those of entry 9.

Various aliphatic acid chlorides were reacted with **2b** in the presence of the [IrCl(cod)]₂/PCy₂(*o*-Tol) catalyst system²³ (Table 4). Acid chlorides (**1f–1**) in entries 1–7 afforded the corresponding β -chloro- α , β -unsaturated ketones **3** in high

Table 3. Effect of Ligands on the Iridium-Catalyzed Addition of Stearoyl Chloride (1d) and Phenylacetyl Chloride (1e) to Cyclohexylacetylene (2b)^a

entry	1	ligand	3	% yield ^b
1	1d	[IrCl(cod)(IPr)] ^c	3db	(29) ^d
2		IMes-HCl/ <i>t</i> -BuOK		trace
3		PPh ₃		0
4		PCy ₃		37
5		PCy ₂ Ph		13
6		PCy ₂ (<i>o</i> -biphenyl)		16
7		XPhos		31
8		RuPhos		0
9		PCy ₂ (<i>o</i> -Tol)		94 (75) ^d
10	1e	[IrCl(cod)(IPr)] ^c	3eb	(18) ^d
11		RuPhos		a complex mixture
12		PCy ₂ (<i>o</i> -Tol)		(89) ^d

^aConditions: **1d** or **1e** (0.50 mmol), **2b** (0.75 mmol), [IrCl(cod)]₂ (0.0125 mmol), ligand (0.025 mmol, P/Ir = 1.0), toluene (1.0 mL), at 60 °C, for 20 h. ^bDetermined by GC analysis by using tetradecane as an internal standard. Z/E = >99/1. ^c[IrCl(cod)(IPr)] (0.025 mmol) was used as the catalyst at 90 °C. ^dIsolated yields in parentheses.

yields. In particular, **1h–j** (entries 3–5) and **1k–l** (entries 6 and 7) would afford thermodynamically stable disubstituted alkenes and conjugated alkenes, respectively, after β -hydrogen elimination. However, even in these cases, the desired adducts (**3hb–lb**) were obtained selectively. Moreover, for arylacetyl chlorides (**1m–t**), the same [IrCl(cod)]₂/PCy₂(*o*-Tol) catalyst system also showed high catalytic activity as observed for phenylacetyl chloride (**1e**) (entry 12, Table 3). The arylacetyl chlorides having electron-rich phenyl (**1m–n**), electron-poor phenyl (**1o–q**), 1-naphthyl (**1r**), 3-thienyl (**1s**), and diphenyl (**1t**) moieties afforded **3mb–tb** in good to high yields (entries 8–15). Phenoxyacetyl chloride (**1u**) also afforded **3ub** in 82% yield (entry 16). The Z-configuration of **3tb** was further confirmed through single-crystal X-ray diffraction.²⁴ Unfortunately, bulky acid chlorides such as pivaloyl chloride and 1-adamantanecarbonyl chloride did not react at all under the present reaction conditions.

Next, various terminal alkynes (**2**) were reacted with **1k** as a representative aliphatic acid chloride at 60 °C, and the corresponding adducts (**3**) were isolated in high yields regio- and stereoselectively (Table 5). 1-Octyne (**2c**) and 3,3-dimethyl-1-butyne (**2d**) smoothly provided **3kc** and **3kd** in high yields without decarbonylation and β -hydrogen elimination (entries 1 and 2). Functionalities such as chloro, ester, and phthalimide can be tolerated in the reaction, and the adducts (**3ke–kh**) were afforded in good yields (entries 3–6). The addition to enyne **2i** successfully proceeded to give **3ki** in 80% yield (entry 7). Phenylacetylene (**2a**) and its derivatives (**2j–n**) also gave the adducts at 90 °C (entries 8–13). Unfortunately, in all of the addition reactions of both the aliphatic acid chlorides and aroyl chlorides, internal alkynes showed very low reactivity and did not provide any of the corresponding product **3**.

Table 4. Addition of Aliphatic Acid Chlorides (1) to 2b^a

2.5 mol % $[\text{IrCl}(\text{cod})]_2$ 5.0 mol % $\text{PCy}_2(o\text{-Tol})$ Toluene At 60 °C, for 20 h				
 $\text{G}-\text{C}(=\text{O})-\text{Cl} + \text{H}-\text{C}\equiv\text{C}-\text{C}_6\text{H}_{11} \longrightarrow \text{G}-\text{C}(=\text{O})-\text{CH}=\text{C}(\text{Cl})-\text{C}_6\text{H}_{11}$ 1				

^aConditions: Acid chlorides (**1**, 0.50 mmol), **2b** (0.75 mmol), [IrCl(cod)]₂ (0.0125 mmol, 2.5 mol %), PCy₂(*o*-Tol) (0.025 mmol, 5.0 mol %), toluene (1.0 mL), at 60 °C, for 20 h. ^bIsolated yields. ^cAt 90 °C.

The products of the addition reaction, β -chloro- α,β -unsaturated ketones **3**, are versatile intermediates in organic synthesis.¹⁴ As was previously reported,¹⁸ **3** obtained from

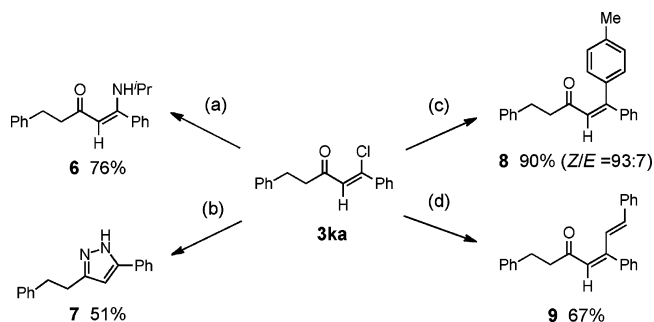
Table 5. Iridium-Catalyzed Addition of **1k** to Terminal Alkynes (**2**)^a

entry		2	3	% yield ^b
1		H≡C-C ₆ H ₁₃ 2c	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₁₃ 3kc	86
2		H≡C- <i>t</i> -Bu 2d	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH- <i>t</i> -Bu 3kd	89
3		H≡C-CH ₂ -CH ₂ -Cl 2e	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-CH ₂ -CH ₂ -Cl 3ke	77
4		H≡C-CH ₂ -CH ₂ -CO ₂ Me 2f	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-CH ₂ -CH ₂ -CO ₂ Me 3kf	76
5		H≡C-CH ₂ -CH ₂ -OAc 2g	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-CH ₂ -CH ₂ -OAc 3kg	79
6		H≡C-CH ₂ -CH ₂ -N ₂ 2h	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-CH ₂ -CH ₂ -N ₂ 3kh	84
7		H≡C-C ₆ H ₁₁ 2i	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₁₁ 3ki	80
8 ^c		H≡C-Ph 2a	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-Ph 3ka	81
9 ^c		H≡C-C ₆ H ₄ -Me 2j	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₄ -Me 3kj	88
10 ^c		H≡C-C ₆ H ₄ -Cl 2k	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₄ -Cl 3kk	75
11 ^c		H≡C-C ₆ H ₄ -OMe 2l	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₄ -OMe 3kl	81
12 ^c		H≡C-C ₆ H ₄ -Br 2m	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₄ -Br 3km	58
13 ^c		H≡C-C ₆ H ₄ -Ph 2n	Ph-CH ₂ -CH ₂ -C(=O)-CH=CH-C ₆ H ₄ -Ph 3kn	78

^aConditions: **1k** (0.50 mmol), **2** (0.75 mmol), [IrCl(cod)]₂ (0.0125 mmol, 2.5 mol %), PCy₂(*o*-Tol) (0.025 mmol, 5.0 mol %), toluene (1.0 mL), at 60 °C, for 20 h. ^bIsolated yields. ^cAt 90 °C.

alkynes bearing methylene unit adjacent to C–C triple bond affords furans.^{25,26} The synthetic utility of **3** was further demonstrated by using **3ka** in Scheme 2. The reaction with isopropylamine and hydrazine cleanly gave the β-amino-α,β-unsaturated ketone **6** and the pyrazole **7**, respectively, via a conjugated substitution reaction.²⁷ The chloro functionality of **3ka** was able to be utilized by the palladium-catalyzed Suzuki–Miyaura coupling reaction²⁸ with *p*-tolylboronic acid to give **8** in 90% yield, containing a small amount of stereoisomers determined by NMR (*Z/E* = 93/7). A similar coupling reaction with *trans*-styrylboronic acid gave a dienyl ketone **9** as a single isomer in 67% yield.

To gain insight into the reaction mechanisms, stoichiometric reactions of an acid chloride with the most active catalysts, [IrCl(cod)(IPr)] and [IrCl(cod)]₂/PCy₂(*o*-Tol), were carried out. First, in a stoichiometric reaction of [IrCl(cod)(IPr)] with an aroyl chloride **1a**, most **1a** (>91% by GC) remained unchanged even at 90 °C for 4 h.¹⁸ However, when an alkyne **2a** was further added into the reaction mixture, most of the **1a**

Scheme 2. Transformation of β-Chloroalkenyl Ketone **3ka**^a

^aConditions: (a) *i*-PrNH₂ (20 equiv), Et₂O, room temperature, 16 h. (b) N₂H₄·H₂O (3 equiv), EtOH, reflux, 5 h. (c) *p*-Tolylboronic acid (1.5 equiv), Pd(OAc)₂ (2.0 mol %), SPhos (5.0 mol %), K₃PO₄ (2.0 equiv), toluene, 100 °C, 18 h. (d) *trans*-Styrylboronic acid (1.5 equiv), Pd(OAc)₂ (2.0 mol %), SPhos (5.0 mol %), K₃PO₄ (2.0 equiv), toluene, 100 °C, 18 h.

was converted to afford **3aa** in 52% yield (eq 1). Thus, oxidative addition of an acid chloride smoothly proceeds in the presence of an alkyne, and then a fast insertion of the alkyne affords **3** without decarbonylation.

In a similar stoichiometric reaction of an aliphatic acid chloride **1d** with [IrCl(cod)]₂/PCy₂(*o*-Tol) (Ir/P/**1d** = 1/1/1) at 60 °C for 2 h, **1d** was converted completely even in the absence of an alkyne (entry 1, Table 6). In the reaction, **5** was

Table 6. Stoichiometric Reaction of [IrCl(cod)]₂/Phosphine (Phosphine = PCy₂(*o*-Tol) or PPh₃) with **1d**^a

[IrCl(cod)] ₂ + phosphine + 1d		2b	% yield ^c	
		toluene at 60 °C, for 2 h	5	3db
entry	phosphine	2b / 1d ^b		
1	PCy ₂ (<i>o</i> -Tol)	0	90	0
2		1	67	12
3		2	45	25
4		4	28	37
5		8	23	43
6		12	19	43
7	PPh ₃	0	68	0
8		1	77	0
9		4	76	0
10		8	75	0

^aConditions: [IrCl(cod)] (25 μmol), PCy₂(*o*-Tol) or PPh₃ (50 μmol), **1d** (50 μmol), toluene (1.0 mL), at 60 °C, for 2 h. ^bMolar ratios of **2b**/**1d**. ^cDetermined by GC analysis.

obtained in 90% yield via decarbonylation and subsequent facile β-hydrogen elimination. From the reaction mixture, no discrete Ir complexes could be isolated. Quite interestingly, when the reaction was carried out in the presence of **2b**, the adduct **3db** was obtained in higher yields as the amount of **2b** increased (entries 2–6). In sharp contrast, employing PPh₃ as the ligand did not afford **3db** at all and β-hydrogen elimination to **5** was prevailing, even when **2b** was used in excess (entries 7–10). This ligand effect is very reminiscent of the catalytic reaction: PCy₂(*o*-Tol) was an excellent ligand to afford **3db** in high yield, while PPh₃ as the ligand did not provide **3db** at all (entries 3 and 9 in Table 3).

Unlike **1d**, the stoichiometric reaction of phenylacetyl chloride (**1e**) with [IrCl(cod)]₂/PCy₂(*o*-Tol) will not undergo

β -hydrogen elimination after decarbonylation, because the resulting species **B** has no β -hydrogens (Scheme 1). Actually, in the reaction at 60 °C, a binuclear (benzyl)(carbonyl)iridium complex **10** was isolated in 90% yield (eq 2). The structure of **10** was confirmed by X-ray diffraction study (Figure 2).²⁴ Here,

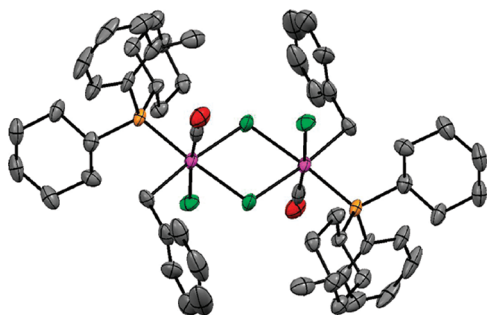
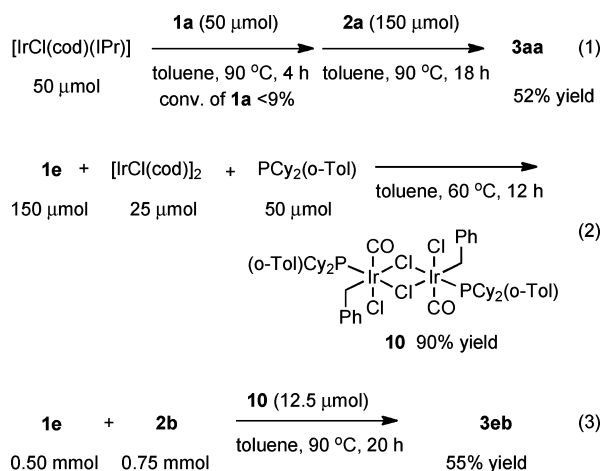
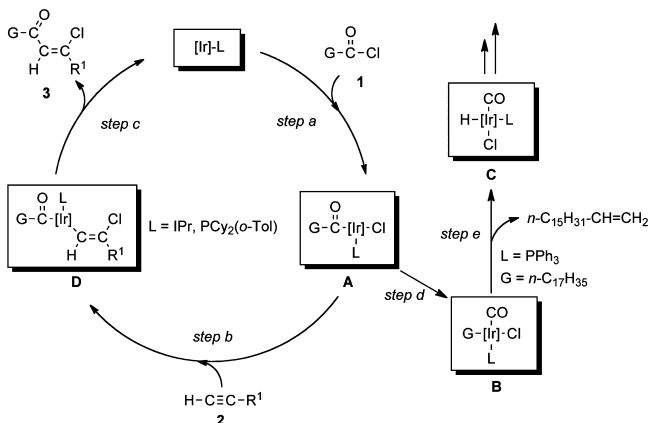


Figure 2. Crystal structure of **10**.

decarbonylation was still fast, and the corresponding phenylacetyl complex was not obtained. However, under the catalytic conditions (with excess alkyne), **10** catalyzed the addition of **1e** to **2b** to provide **3eb** without decarbonylation in 55% yield (eq 3).



Scheme 3. Plausible Reaction Mechanism



With these results obtained in eqs 1–3 and Table 6, a possible catalytic cycle is shown in Scheme 3. Oxidative addition of acid chlorides (**1**) to an active catalyst species $[\text{Ir}]\text{L}$

affords adducts **A** (step a). For successful insertion of alkynes (**2**) to afford alkenyl intermediates (**D**)²⁹ without decarbonylation, an appropriate ligand is crucial on the iridium center. For aroyl derivatives of **A**, an IPr ligand is most suitable (entries 7 and 8 in Table 1; Table 2), while for **A** from aliphatic acid chlorides $\text{PCy}_2(\text{o-Tol})$ is requisite (entries 9 and 12 in Table 3; Tables 4 and 5). Fast reductive elimination of **D** then provides β -chloro- α,β -unsaturated ketones **3**, and the catalytic cycle is closed to regenerate the catalytic species.

As shown in eq 1, oxidative addition of aroyl chlorides to $[\text{Ir}]\text{L}$ ($\text{L} = \text{IPr}$) (step a) occurs in the presence of alkynes **2**. Insertion of **2** to **A** (step b) is much faster than decarbonylation (step d). On the other hand, as indicated in eq 2, oxidative addition of aliphatic acid chlorides occurs in the absence of **2**, but the adduct **A** could not be isolated due to fast decarbonylation (step d) followed by facile β -hydrogen elimination (step e). Here, $\text{PCy}_2(\text{o-Tol})$ is a unique ligand under the catalytic conditions (in the presence of excess **2**). As indicated by entries 1–6 in Table 6, $\text{PCy}_2(\text{o-Tol})$ ligand enhances insertion of **2** (step b) more efficiently than decarbonylation (step d). Other ligands such as PPh_3 do not have such ability, and decarbonylation followed by β -hydrogen elimination proceeded considerably. Thus, in the present iridium-catalyzed reaction, the ligand with good coordination ability and suitable steric bulk is indispensable for the selective addition of **1** to **2**.

CONCLUSION

Various aroyl chlorides and aliphatic acid chlorides (**1**) are successfully added to terminal alkynes (**2**) to afford useful (*Z*)- β -chloro-alkenyl ketones (**3**) regio- and stereoselectively in the presence of a catalytic amount of iridium complexes, $[\text{IrCl}(\text{cod})(\text{IPr})]$ or $[\text{IrCl}(\text{cod})]_2/\text{PCy}_2(\text{o-Tol})$. The present catalytic addition reaction proceeds smoothly with suppression of undesired decarbonylation and β -hydrogen elimination. The ligands in the catalytic system play a key role in determining the selectivity of the addition reaction.

EXPERIMENTAL SECTION

Instrumentation and Chemicals. All manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares on a dual-manifold Schlenk line. Unless otherwise noted, materials obtained from commercial supplier were used without further purification. Acid chlorides **1q**, **1r**, and **1s** were prepared from the corresponding carboxylic acid and thionyl chloride,³⁰ and purified by distillation under vacuum. All solvents were dried and purified by usual procedures.³¹ ^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). IR spectra were obtained on a SHIMADZU FTIR-8300 spectrometer. EI-MS was 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. $\times$ 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 60F254.

General Procedure of the Addition of Aroyl Chlorides (1**) to Terminal Alkynes (**2**) without Decarbonylation (Table 2).** $\text{IrCl}(\text{cod})(\text{IPr})$ (18 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. A degassed toluene (1.0 mL) was then added to the flask. An aryl 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 being cooled to room temperature, the mixture was evaporated, and the product (**3**) was isolated by silica gel column chromatography.

General Procedure of the Addition of Aliphatic Acid Chlorides (1**) to Terminal Alkynes (**2**) (Tables 4 and 5).** $[\text{IrCl}(\text{cod})]_2$ (8.4 mg, 0.0125 mmol) and $\text{PCy}_2(o\text{-Tol})$ (7.2 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. Toluene (1.0 mL) was then added to the flask, and the resultant solution was stirred at room temperature for 10 min. An aliphatic 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 being cooled to room temperature, the mixture was evaporated, and the product (**3**) was isolated by silica gel column chromatography.

Stoichiometric Reaction in Table 6. $[\text{IrCl}(\text{cod})]_2$ (17 mg, 0.025 mmol) and $\text{PCy}_2(o\text{-Tol})$ (14 mg, 0.050 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. Toluene (1.0 mL) was then added to the flask, and the resultant solution was stirred at room temperature for 10 min. Next, **1d** (0.050 mmol) and **2b** (0, 0.050, 0.10, 0.20, 0.40, or 0.60 mmol: **2b**/**1d** = 0, 1, 2, 4, 8, or 12) and tetradecane (0.050 mmol) as an internal standard were added to the flask, and the mixture was stirred at 60 °C for 2 h under an argon atmosphere. After being cooled to room temperature, the reaction mixture was diluted with diethyl ether (2.0 mL), and the yields of **3db** and 1-heptadecene (**5**) were determined by GC analysis.

Stoichiometric Reaction in Equation 1. To a 10 mL Schlenk flask with a reflux condenser was added $\text{IrCl}(\text{cod})(\text{IPr})$ (36 mg, 0.050 mmol). The flask was evacuated and backfilled with argon three times. A degassed toluene (1.0 mL) was then 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 , 0.10 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, **2a** (8.2 μL , 0.075 mmol) was added to the reaction mixture, and the reaction was carried out at 90 °C for 18 h. After being cooled to room temperature, the reaction mixture was diluted with diethyl ether (2.0 mL). GC analysis showed **3aa** was obtained in 52% yield.

Stoichiometric Reaction in Equation 2. $[\text{IrCl}(\text{cod})]_2$ (34 mg, 0.050 mmol) and $\text{PCy}_2(o\text{-Tol})$ (29 mg, 0.10 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. Next, toluene (1.0 mL) was added to the flask, and the resultant solution was stirred at room temperature for 10 min. Phenylacetyl chloride (**1e**) (0.30 mmol) was added to the flask, and the mixture was stirred at 60 °C for 12 h under an argon atmosphere. After being cooled to room temperature, the mixture was evaporated, and the crude product was washed with diethyl ether (1 mL $\times$ 3) to give off-white solids of $[\text{IrCl}_2(\text{CO})\{\text{PCy}_2(o\text{-Tol})\}(\text{CH}_2\text{Ph})]_2$ (**10**) (54.6 mg, 81% yield).

■ ASSOCIATED CONTENT

■ Supporting Information

Experimental procedures and characterization of the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

ytsuji@scl.kyoto-u.ac.jp

Present Address

[†]Department of Chemistry, Faculty of Science, Hokkaido University, Japan.

■ ACKNOWLEDGMENTS

This work was supported by a Grant-in-Aid for Scientific Research on Innovative Areas ("Organic synthesis based on reaction integration" and "Molecular activation directed toward straightforward synthesis") from MEXT, Japan, and in part by the Mitsubishi Foundation. T.I. is grateful for a Research Fellowship of JSPS for Young Scientists. T.F. acknowledges the The Naito Foundation Natural Science Scholarship.

■ REFERENCES

- (1) (a) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695–705. (b) Sheldon, R. A. *Pure Appl. Chem.* **2000**, *72*, 1233–1246. (c) Trost, B. M. *Science* **1991**, *254*, 1471–1477.
- (2) For a review, see: Fujihara, T.; Iwai, T.; Terao, J.; Tsuji, Y. *Synlett* **2010**, 2537–2548.
- (3) Recent reviews, see: (a) Willis, M. C. *Chem. Rev.* **2010**, *110*, 725–748. (b) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222–234. (c) Jun, C.-H.; Jo, E.-A.; Park, J.-W. *Eur. J. Org. Chem.* **2007**, 1869–1881. (d) Fu, G. C. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, A., Ed.; Wiley-VCH: Weinheim, 2005; pp 79–91.
- (4) (a) Garraalda, M. A. *Dalton Trans.* **2009**, 3635–3645. (b) Ohno, K.; Tsuji, J. *J. Am. Chem. Soc.* **1968**, *90*, 99–107. (c) Milstein, D. *Organometallics* **1995**, *14*, 1549–1551. (d) Wang, K.; Emge, T. J.; Goldman, A. S.; Li, C.; Nolan, S. P. *Organometallics* **1995**, *14*, 4929–4936.
- (5) For decarbonylation of aldehydes, see: (a) Iwai, T.; Fujihara, T.; Tsuji, Y. *Chem. Commun.* **2008**, 6215–6217. (b) Fristrup, P.; Kreis, M.; Palmelund, A.; Norrby, P.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 5206–5215. (c) Kreis, M.; Palmelund, A.; Bunch, L.; Madsen, R. *Adv. Synth. Catal.* **2006**, *348*, 2148–2154. (d) Doughty, D. H.; Pignolet, L. H. *J. Am. Chem. Soc.* **1978**, *100*, 7083–7085. (e) Ohno, K.; Tsuji, J. *J. Am. Chem. Soc.* **1968**, *90*, 99–107.
- (6) (a) Coulter, M. M.; Dornan, P. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 16042–16043. (b) Kundu, K.; McCullagh, J. V.; Morehead, A. T. Jr. *J. Am. Chem. Soc.* **2005**, *127*, 16042–16043. (c) Sato, Y.; Ohnishi, Y.; Mori, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1218–1221. (d) Tanaka, K.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 8078–8079. (e) Tanaka, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 11492–11493. (f) Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821–1830. (g) Larock, R. C.; Oertle, K.; Potter, G. F. *J. Am. Chem. Soc.* **1980**, *102*, 190–197. (h) Sakai, K.; Ishiguro, Y.; Funakoshi, K.; Ueno, K.; Suemune, H. *Tetrahedron Lett.* **1984**, *25*, 961–964.
- (7) (a) Legrand, C.; Castanet, Y.; Mortreux, A.; Petit, F. *J. Chem. Soc., Chem. Commun.* **1994**, 1173–1174. (b) Kondo, T.; Akazome, M.; Tsuji, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286. (c) Lin, I. J. B.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1989**, 248–249. (d) Tsuji, Y.; Yoshii, S.; Ohsumi, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1987**, *331*, 379–385.
- (8) (a) Nakao, Y.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 10024–10026. (b) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222–234. (c) Jun, C.-H. *Chem. Soc. Rev.* **2004**, *33*, 610–618. (d) Ko, S.; Na, Y.; Chang, S. *J. Am. Chem. Soc.* **2002**, *124*, 750–751. (e) Imai, M.; Tanaka, M.; Tanaka, K.; Yamamoto, Y.; Imai-Ogata, N.; Shimowatari, M.; Nagumo, S.; Kawahara, N.; Suemune, H. *J. Org. Chem.* **2004**, *69*, 1144–1150. (f) Willis, M. C.; McNally, S. J.; Beswick, P. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 340–343.
- (9) Ru-catalyzed hydroacylations of alkynes and dienes without directing groups to suppress decarbonylation were described, see: (a) Shibahara, F.; Bower, J. F.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 14120–14122. (b) Williams, V. M.; Leung, J. C.; Patman, R. L.; Krische, M. J. *Tetrahedron* **2009**, *65*, 5024–5029.

- (10) The use of carboxylic anhydrides in reductive hydroacylation of alkenes without directing groups employing a rhodium catalyst was reported. Hong, Y.-T.; Barchuk, A.; Krische, M. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6885–6888.
- (11) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*, 4th ed.; John Wiley and Sons: Hoboken, NJ, 2005; pp 183–206.
- (12) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 5.
- (13) (a) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941–6946. (b) Obora, Y.; Tsuji, Y.; Kawamura, T. *J. Am. Chem. Soc.* **1995**, *117*, 9814–9821. (c) Liu, J.; Deng, C.; Tseng, N.-W.; Chan, C. Y. K.; Yue, Y.; Ng, J. C. Y.; Lam, J. W. Y.; Wang, J.; Hong, Y.; Sung, H. H. Y.; Williams, I. D.; Tang, B. Z. *Chem. Sci.* **2011**, *2*, 1850–1859. (d) Zhao, X.; Yu, Z. *J. Am. Chem. Soc.* **2008**, *130*, 8136–8137. (e) Sugihara, T.; Satoh, T.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4672–4674. (f) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638.
- (14) Pohland, A. E.; Benson, W. R. *Chem. Rev.* **1966**, *66*, 161–197.
- (15) (a) Kashiwabara, T.; Fuse, K.; Hua, R.; Tanaka, M. *Org. Lett.* **2008**, *10*, 5469–5472. (b) Kashiwabara, T.; Kataoka, K.; Hua, R.; Shimada, S.; Tanaka, M. *Org. Lett.* **2005**, *7*, 2241–2244. (c) Kashiwabara, T.; Tanaka, M. *Adv. Synth. Catal.* **2011**, *353*, 1485–1490.
- (16) As for chloroformates^{16a,b} and chlorooxoacetate^{16c} as a substrate in a rhodium-catalyzed addition to alkynes, see: (a) Beak, J. Y.; Lee, S. I.; Sim, S. H.; Chung, Y. K. *Synlett* **2008**, 551–554. (b) Hua, R.; Shimada, S.; Tanaka, M. *J. Am. Chem. Soc.* **1998**, *120*, 12365–12366. (c) Hua, R.; Onozawa, S.-y.; Tanaka, M. *Chem.-Eur. J.* **2005**, *11*, 3621–3630.
- (17) (a) Price, C. C.; Pappalardo, J. A. *J. Am. Chem. Soc.* **1950**, *72*, 2613–2615. (b) Martens, H.; Janssens, F.; Hoornaert, G. *Tetrahedron* **1975**, *31*, 177–183. (c) Zhou, H.; Zeng, C.; Ren, L.; Liao, W.; Huang, X. *Synlett* **2006**, 3504–3506. (d) Wang, B.; Wang, S.; Li, P.; Wang, L. *Chem. Commun.* **2010**, 5891–5893. (e) Hosseini-Savari, M.; Mardaneh, Z. *Bull. Chem. Soc. Jpn.* **2011**, *84*, 778–782. (f) Snelders, D. J. M.; Dyson, P. J. *Org. Lett.* **2011**, *13*, 4048–4051.
- (18) The addition of aroyl chlorides to alkynes was preliminarily reported, see: Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6668–6669.
- (19) Hegedus, L. S.; Söderberg, B. C. G. *Transition Metals in the Synthesis of Complex Organic Molecules*, 3rd ed.; University Science Books: Sausalito, CA, 2010.
- (20) PCy₂(*o*-Tol), dicyclohexyl(2-methylphenyl)phosphine, is commercially available from Aldrich.
- (21) Biscoe, M. R.; Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 6686–6687 and references cited therein.
- (22) Kelly, R. A.; Clavier, H.; Giudice, S.; Scott, N. M.; Stevens, E. D.; Bordner, J.; Samardjiev, I.; Hoff, C. D.; Cavallo, L.; Nolan, S. P. *Organometallics* **2008**, *27*, 202–210.
- (23) [IrCl(cod){PCy₂(*o*-Tol)}] must be generated in situ according to the relevant literature, see: Diebolt, O.; Fortman, G. C.; Clavier, H.; Slawin, A. M. Z.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Nolan, S. P. *Organometallics* **2011**, *30*, 1668–1676.
- (24) See the Supporting Information for details.
- (25) For recent catalytic synthesis of furans, see: (a) Zhang, M.; Jiang, H.-F.; Neumann, H.; Beller, M.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2009**, *48*, 1681–1684. (b) Dudnik, A. S.; Sromek, A. W.; Rubina, M.; Kim, J. T.; Kel'in, A. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2008**, *130*, 1440–1452 and references cited therein.
- (26) An allenic ketone was not obtained in the reaction of β -chloro- α,β -unsaturated ketone with a base such as *t*-BuOK.
- (27) Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*; Oxford University: Oxford, 2001; Chapter 23, pp 585–588.
- (28) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483. (b) Miyaura, N. In *Metal-Catalyzed Cross-Coupling Reaction*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 41–123.
- (29) Miura^{13a} and Tanaka¹⁵ suggested an insertion of alkynes (2) into metal(Rh)–Cl bonds. However, the insertion of 2 into the aroyl–iridium bonds cannot be ruled out.
- (30) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; Wiley-VCH: New York, 1999; p 1929.
- (31) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Butterworth-Heinemann: Oxford, U.K., 2003.