Bull. Chem. Soc. Jpn., 75, 1333–1345 (2002)

Palladium-Catalyzed Direct Conversion of Carboxylic Acids into Ketones with Organoboronic Acids Promoted by Anhydride Activators

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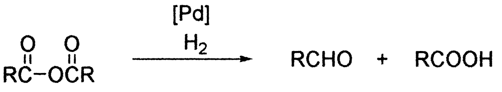
(Received November 5, 2001)

Various carboxylic acids are catalytically converted into ketones on treatment with organoboron compounds in the presence of activators and palladium catalysts. Detailed examination of factors influencing the yield of ketone formation revealed the following characteristics of the reactions: (a) Palladium complexes containing tertiary phosphine ligands, particularly triphenylphosphine and tricyclohexylphosphine, are most effective among the palladium complexes; (b) Dioxane and THF are suitable as the solvent; (c) Dimethyl dicarbonate is required as the activator to obtain ketones in high yields. The process provides a general, versatile, synthetic method to produce various symmetrical and unsymmetrical ketones with aromatic, aliphatic, and heterocyclic groups. The mechanism proposed for the catalytic process involves (i) exchange reaction of the carboxylic acid employed with dimethyl dicarbonate added as the activator to form a mixed anhydride of the carboxylic acid and mono methyl ester of carbonic acid; (ii) oxidative addition of the mixed anhydride to zerovalent palladium species to give an (acyl)(methyl carbonato)palladium species; (iii) decarboxylation of the methyl carbonato ligand to give (acyl)(methoxo)palladium species; (iv) transmetallation of the (acyl)(methoxo)palladium species with an arylboronic acid to give an (acyl)(aryl)palladium species; and (v) reductive elimination of the (acyl)(aryl)palladium species to liberate the coupling product of the acyl and aryl ligands with regeneration of the Pd(0) species. Not only homogeneous catalyst systems but also heterogeneous systems were found to give ketones under mild conditions. On the basis of the present study involving the acyl(methoxo)palladium complexes generated in the reaction mixture of carboxylic acids with dimethyl dicarbonate on reaction with Pd(0) complexes, we also developed a new catalytic process to convert carboxylic acids with terminal alkynes into *α*, *β*-alkynyl ketones under similar conditions.

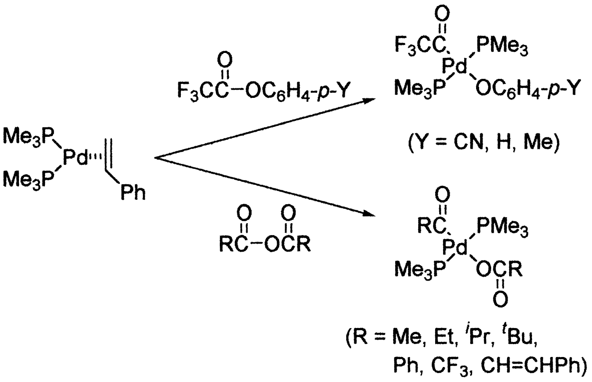
Among palladium-catalyzed processes to perform the C–C bond formation in organic synthesis,[1] cross-coupling reactions of aryl and alkenyl halides with various organometallic compounds of non-transition metals[2] have provided useful methodology in organic synthesis together with arylation of olefins (Mizoroki–Heck processes).[3] However, both processes entail intrinsic problems of using organic halides as substrates for preparation of products without halogen. Thus finding more atom-efficient methodology is needed for reducing waste. We have been concerned with development of an alternative method to replace organic halides with oxygen-containing compounds as the starting compounds on the basis of the information gained in examination of the C–O bond cleavage processes promoted by transition metal complexes.[4]

In previous studies we have found that aryl trifluoroacetates[5] and carboxylic anhydrides[6] readily undergo the oxidative addition reaction to afford acylpalladium carboxylate and aryloxide complexes (Scheme 1).

The acylpalladium carboxylate complexes were found to react with molecular hydrogen, releasing aldehydes and carboxylic acids. Utilizing the behavior of the acylpalladium complexes to release aldehyde we could develop a palladium-catalyzed process to synthesize aldehydes and carboxylic acids from carboxylic anhydrides (Eq. 1).[6]

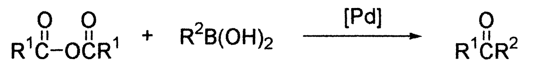


$$\mathrm{R\overset{O}{\overset{\|}{C}}-O\overset{O}{\overset{\|}{C}}R} \xrightarrow{\substack{[\mathrm{Pd}]\\ \mathrm{H_2}}} \mathrm{RCHO} + \mathrm{RCOOH} \qquad (1)$$



Scheme 1. Cleavage of C–O bond in aryl trifluoroacetates and carboxylic anhydrides.

As another direction of application of the concept of the C–O bond cleavage to give acylpalladium complexes, we conceived of the conversion of the acylpalladium intermediates into ketones. Having found that the acylpalladium complexes react with arylboronic acids to produce ketones, we could develop a new catalytic method of synthesizing unsymmetrical ketones from carboxylic anhydrides using arylboronic acids as arylation reagents (Eq. 2).[7]



$$\mathrm{R^1\overset{O}{\overset{\|}{C}}-O\overset{O}{\overset{\|}{C}}R^1} + \mathrm{R^2B(OH)_2} \xrightarrow{[\mathrm{Pd}]} \mathrm{R^1\overset{O}{\overset{\|}{C}}R^2} \qquad (2)$$

Utilization of the ready cleavage of the C–O bond in aryl perfluoroalkanecarboxylates combined with transmetallation using arylboronic acids also led to the catalytic synthesis of fluorine-containing unsymmetrical ketones.[8]

These catalytic processes have provided new routes to aldehydes and ketones starting from carboxylic anhydrides. However, these processes still include shortcomings such as the need for prior preparations of anhydrides.

Our studies on reactions of different carboxylic anhydrides with Pd(0) complexes revealed that the acyl unit of less steric demand in anhydrides showed higher reactivity in their oxidative addition process to give the acylpalladium intermediate. On the basis of such information, we have developed a catalytic process of synthesizing aldehydes directly from carboxylic acids without prior preparation of carboxylic anhydrides (Eq. 3).[9]

$$\mathrm{RCOOH} + \mathrm{H_2} \xrightarrow[\ ]{\text{Pd catalyst} \atop ({}^t\mathrm{BuCO})_2\mathrm{O}} \mathrm{RCHO} \qquad (3)$$

The concept for realizing the palladium-catalyzed direct conversion of a carboxylic acid into an aldehyde is based on the utilization of an exchange process of a carboxylic acid with a carboxylic anhydride of less reactivity, such as pivalic anhydride (2,2-dimethylpropanoic anhydride). Addition of the bulky pivalic anhydride to the carboxylic acid would lead to the mixture of mixed anhydride and symmetrical anhydrides. The less hindered acyl unit in the anhydride produced from the exchange reaction would react preferentially with Pd(0) complex to undergo the selective acyl-O bond cleavage to generate the acylpalladium complex that reacts preferentially with hydrogen liberating the aldehyde from the carboxylic acid employed.

In fact, by adding pivalic anhydride to the reaction system containing the carboxylic acid and the palladium catalyst under hydrogen pressure, we could obtain aldehydes in high yields selectively in a one-pot process under mild conditions.[9]

The success of using pivalic anhydride as an activator in combination with carboxylic acids to form mixed anhydrides to accomplish the selective C–O bond cleavage of the carboxylic acids prompted us examine the applicability of a similar strategy to ketone synthesis.

Ketones occupy pivotal positions as intermediates in organic synthesis as well as end products for various commercial uses. Although quite a variety of synthetic methods are available, most methods entail some shortcomings in efficiency and leave some room for improvement from the environmental viewpoint. For example, palladium-catalyzed oxidation of olefins (Wacker oxidation) has been extensively used for production of ketones in laboratory synthesis as well as in industrial processes.[10] However, applicable olefins are limited and regioselectivity of ketones obtained leaves a problem. Many useful reactions are known in partial oxidation of secondary alcohols to ketones, such as the Swern oxidation,[11] and oxidation by heavy metal salts such as PCC[12] and MnO_2.[13] However, in these processes stoichiometric amounts of oxidizing agents are required, with concomitant formation of undesirable by-product(s). The Friedel–Crafts acylation reactions,[14] which are among the most important processes for the synthesis of aromatic ketones, are generally carried out by using more than a stoichiometric amount of anhydrous aluminum trichloride as a Lewis acid. From an industrial point of view, the reaction is less desirable because of the highly corrosive conditions and the concomitant formation of a large amount of waste. In addition, Friedel–Crafts reactions display ortho and para selectivity and are not suitable for preparation of aryl ketones with a meta substituent. Reaction of organometallic reagents of electropositive metals such as lithium and magnesium with carboxylic acid derivatives provides a convenient laboratory method for the synthesis of ketones,[15] but the reactions have to be carried out at low temperature to avoid the formation of the tertiary alcohols. In addition, the process and Friedel–Crafts acylation reactions generally require the prior preparation of more reactive carboxylic acid derivatives such as acid chlorides, acid anhydrides, and amides. Carboxylic acid themselves are not usually employed as the materials for these reactions.[14,15]

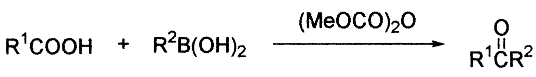
Some methods for synthesis of ketones from carboxylic acid themselves are known.[16] However, most of these reactions have limitations in their applicability and some of the processes are not environmentally benign or need to be performed under drastic experimental conditions.

Recently palladium-catalyzed cross-coupling reactions have gained considerable attention as routes to ketones.[15] Among these palladium-catalyzed cross-coupling processes, the protocol using organoboron compounds (Suzuki–Miyaura process)[17] has proved useful in giving the desired ketones.[7,8,18,19] The process usually gives the coupling products in high yields, tolerates functional groups, and shows excellent stereochemistry. In addition, most organoboron compounds are nontoxic, inert to air and moisture, thermally stable, and can be recrystallized from water or alcohols.

Representative palladium-catalyzed preparative methods of ketones are (i) carbonylative cross-coupling of haloarenes with organoboron compounds[18] and (ii) cross-coupling reaction of acyl halides with various organoboron compounds.[19] However, these methods also entail problems with the requirement of prior preparation of alkyl or acyl halides and the necessity of using a stoichiometric amount of a base. Thus these processes are not applicable to the synthesis of ketones sensitive to a base, besides the inherent environmental problems and low atom efficiency.

Another new route to ketone synthesis without using a base has been recently developed by Liebeskind.[20] The process provides a convenient new route to ketones although requirements of the prior synthesis of thioesters[21,22] and of addition of a stoichiometric amount of copper carboxylate leave room for improvement.

We have recently reported in a communication that carboxylic acid themselves can be catalytically converted into the corresponding ketones, usually in excellent yields, on treatment with arylboronic acids in the presence of dimethyl dicarbonate and palladium catalysts (Eq. 4).[23]

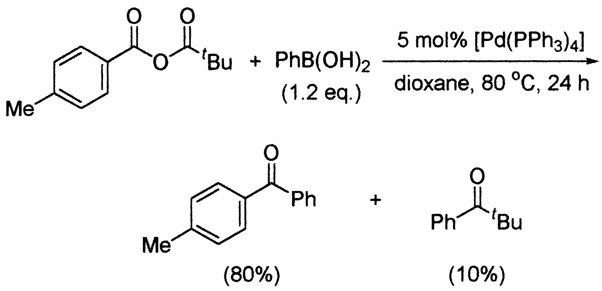


$$\mathrm{R^1COOH} + \mathrm{R^2B(OH)_2} \xrightarrow{[\mathrm{Pd}] \atop (\mathrm{MeOCO})_2\mathrm{O}} \mathrm{R^1}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{R^2} \qquad (4)$$

In the present paper, we summarize the full details of the catalytic process and discuss the applicability of the process.

Results

Catalytic Processes to Prepare Ketones from Carboxylic Acids and Organoboron Compounds. Before attempting the direct conversion of carboxylic acids into ketones using arylboronic acids, we examined relative reactivities of the acyl units in a mixed anhydride having one bulky acyl and the other less bulky aroyl units, as we briefly mentioned in the previous report on catalytic conversion of carboxylic anhydrides into ketones.[7] Treatment of pivalic *p*-toluic anhydride with 1.2 mol amt. of phenylboronic acid in the presence of [Pd(PPh_3)$_4$] at 80 °C for 24 hours yielded 4-methylbenzophenone and 2,2-dimethylpropiophenone in 80% and 10% yields, respectively (Eq. 5).

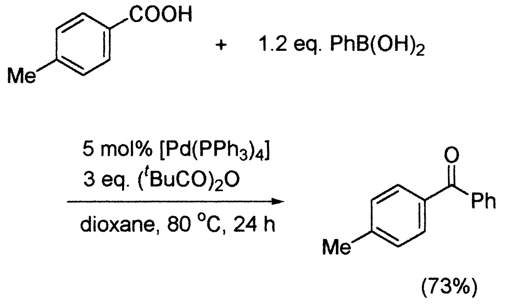


(5)

The result suggests that the less bulky acyl part in the mixed anhydride reacted preferentially with the palladium complex in the catalytic system.

On the basis of the above result, we designed a catalytic process to convert carboxylic acids with organoboron compounds into ketones by combining the exchange process of the carboxylic acids with a less reactive, bulky carboxylic anhydride such as pivalic anhydride, as shown in Scheme 2.

The conceived catalytic process consists of several elementary processes: (i) the mixture of carboxylic acid and pivalic anhydride undergoes exchange of the acyl entities to give a mixed anhydride;[24] (ii) oxidative addition of the mixed anhydride to a zerovalent palladium complex **A** with the regioselective C–O bond cleavage gives acyl(trimethylacetato)palladium species **B**; (iii) transmetallation of **B** with an arylboronic acid gives an acyl(aryl)palladium species **C**; and (iv) reductive elimination of the acyl and the aryl ligands produces ketone as the coupling product regenerating the Pd(0) species, which further carries the catalytic cycle. In fact, treatment of *p*-toluic acid with phenylboronic acid at 80 °C in dioxane in the presence of pivalic anhydride and 0.05 molar amount of [Pd(PPh_3)$_4$] per *p*-toluic acid for 24 h gave 73% yield of 4-methylbenzophenone (Eq. 6).



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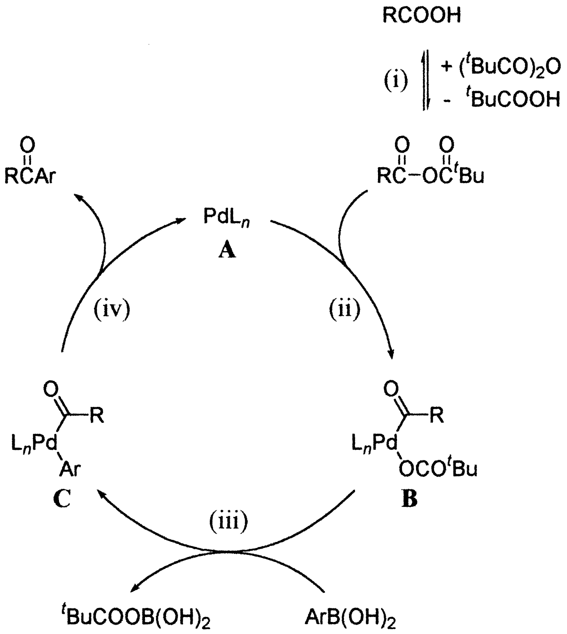


Scheme 2. Catalytic cycle for the formation of ketones.

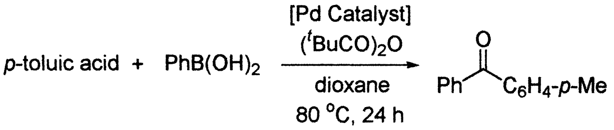
Yields of ketones are influenced by various factors including the nature of catalyst, solvent, temperature, activator, and substrate (carboxylic acids as well as organoboron compounds). We examined the effect of each of these factors on the ketone yields.

(a) Examination of Catalyst Systems. Various palladium catalysts with tertiary phosphine ligands proved effective in synthesizing ketones. Table 1 summarizes activities of various palladium catalysts in reactions of *p*-toluic acid with 1.2 mol amt. of phenylboronic acid at 80 °C in dioxane in the presence of 3 mol amt. of pivalic anhydride per *p*-toluic acid.

Among various palladium complexes examined, [Pd(PCy_3)$_2$] having bulky and electron-donating tricyclohexylphosphine ligands proved to serve as the most effective catalyst for the ketone synthesis when pivalic anhydride was employed as the activator (Run 2). The triphenylphosphine-coordinated Pd(0) complex, [Pd(PPh_3)$_4$], also demonstrated a comparable activity (Run 1). Although Pd(0) is considered to serve as the active species in the catalytic system, it is not necessary to use a phosphine-coordinated palladium(0) complex itself as the catalyst.[25] Use of palladium(II) acetate in combination with three to four molar amounts of PPh_3 per Pd(OAc)$_2$ gave good yields of 4-methylbenzophenone (Runs 4 and 5), but further increase in the amount of triphenylphosphine seems to have some inhibition effect (Run 3). Decrease in the amount of PPh_3 below two molar amounts per palladium acetate caused a decrease in the ketone yield (Run 6). The system using [Pd(dba)$_2$] in combination with 3 to 4 mol amt. of PPh_3 (Runs 7 and 8) showed less activity than the system using Pd(OAc)$_2$ and PPh_3. Palladium(II) acetate in combination with monodentate tertiary phosphines such as tri-*p*-methoxyphenylphosphine and tributylphosphine were moderately effective (Runs 9 and 11). The presence of four molar amounts of tertiary phosphine ligand such as tri-2-furylphosphine caused a lower yield of the ketone (Run 10).

Employment of ditertiary phosphine ligand such as 1,1′-

Table 1. Effect of Homogeneous Catalysts on the Cross-Coupling Reaction of *p*-Toluic Acid with Phenylboronic Acid in the Presence of $(^t\mathrm{BuCO})_2\mathrm{O}$



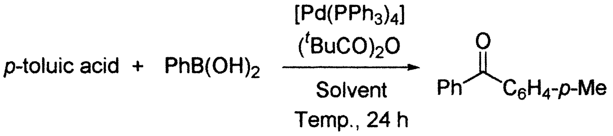
Rum[a)]	Pd-catalyst	Yield/%[b)]
1	$[\mathrm{Pd(PPh_3)_4}]$	73
2	$[\mathrm{Pd(PCy_3)_2}]$	80
3	$\mathrm{Pd(OAc)_2 + 5PPh_3}$	58
4	$\mathrm{Pd(OAc)_2 + 4PPh_3}$	67
5	$\mathrm{Pd(OAc)_2 + 3PPh_3}$	64
6	$\mathrm{Pd(OAc)_2 + 2PPh_3}$	25
7	$\mathrm{[Pd(dba)_2] + 4PPh_3}$	34
8	$\mathrm{[Pd(dba)_2] + 3PPh_3}$	37
9	$\mathrm{Pd(OAc)_2 + 4P(}p\mathrm{\text{-}MeOC_6H_4)_3}$	60
10	$\mathrm{Pd(OAc)_2}$ + 4P(2-furyl)$_3$	11
11	$\mathrm{Pd(OAc)_2 + 2P^{\mathit{n}}Bu_3}$	42
12	$\mathrm{[Pd(dba)_2]}$ + 1DPPF[c)]	46
13	$\mathrm{Pd(OAc)_2}$	7
14	$\mathrm{[Pd(dba)_2]}$	0

a) Typical conditions: a mixture containing *p*-toluic acid (1 mmol), phenylboronic acid (1.2 mmol), pivalic anhydride (3.0 mmol), palladium catalyst (0.05 mmol), and dioxane (5 cm^3) was stirred in a Schlenk tube under argon at 80 °C for 24 h.

b) Determined by GC using $^n\mathrm{C_{14}H_{30}}$ as an internal standard.

c) DPPF is 1, 1′-bis (diphenylphosphino) ferrocene.

Table 2. Effects of Solvents and Temperature on the Cross-Coupling Reactions of *p*-Toluic Acid with Phenylboronic Acid in the Presence of $(^t\mathrm{BuCO})_2\mathrm{O}$



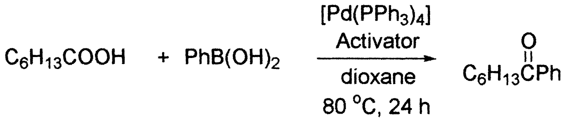
Rum[a)]	Temp/°C	Solvent	Yield/%[b)]
1	r. t.	dioxane	5
2	60	dioxane	47
3	80	dioxane	73
4	100	dioxane	71
5	reflux	THF	68
6	reflux	acetone	44
7	80	toluene	38
8	80	NMP[c)]	47
9	reflux	hexane	5

a) Typical conditions: a mixture containing *p*-toluic acid (1 mmol), phenylboronic acid (1.2 mmol), pivalic anhydride (3.0 mmol), $[\mathrm{Pd(PPh_3)_4}]$ (0.05 mmol), and solvent (5 cm^3) was stirred in a Schlenk tube under argon for 24 h.

b) Determined by GC using $^n\mathrm{C_{14}H_{30}}$ as an internal standard.

c) *N*-methyl-2-pyrrolidinone.

Table 3. Effects of Activator on the Cross-Coupling Reaction of Heptanoic Acid with Phenylboronic Acid



Rum[a)]	Activator	Mol amt.	$\mathrm{C_6H_{13}COPh}$/%[b)]
1	$(^t\mathrm{BuCO})_2\mathrm{O}$	3	83
2	$\mathrm{Ac_2O}$	3	12
3	$(^t\mathrm{BuOCO})_2\mathrm{O}$	3	67
4	$\mathrm{(MeOCO)_2O}$	3	95
5	$\mathrm{(MeOCO)_2O}$	1.2	95
6	$\mathrm{(MeOCO)_2O}$	1	75

a) Typical conditions: a mixture containing hexanoic acid (1 mmol), phenylboronic acid (1.2 mmol), activator (1.0–3.0 mmol), $[\mathrm{Pd(PPh_3)_4}]$ (0.02 mmol), and dioxane (5 cm^3) was stirred in a Schlenk tube under argon at 80 °C for 24 h.

b) Determined by GC using $^n\mathrm{C_{14}H_{30}}$ as an internal standard.

bis(diphenylphosphino)ferrocene (DPPF) with $\mathrm{Pd(OAc)_2}$ also gave a moderate yield of the ketone (Run 12). Palladium complexes such as $\mathrm{Pd(OAc)_2}$ and $\mathrm{[Pd(dba)_2]}$ without tertiary phosphine ligands showed poor or no catalytic activity in the catalyst systems (Runs 13 and 14).

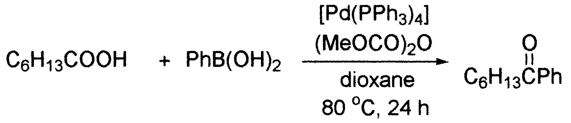
(b) Effects of Solvent and Temperature. Table 2 shows the effects of reaction temperature and of solvents employed. The reaction catalyzed by $[\mathrm{Pd(PPh_3)_4}]$ was slow at room temperature in dioxane (Run 1). Raising the reaction temperature to 60 °C and to 80 °C gave higher yields of ketone, whereas at the still higher temperature of 100 °C a slight decrease in the yield was noted (Runs 2 – 4).

Runs 5 – 9 show the effects of variation of solvents in the catalytic reaction. Higher yields can be obtained when dioxane or THF was employed as a solvent (Runs 3 – 5). Employment of acetone, toluene and 1-methyl-2-pyrrolidinone (NMP) gave moderate yields (Runs 6 – 8), whereas hexane was not suitable as solvent (Run 9).

(c) Effects of Activator. We next examined the effects of various activators for the ketone synthesis from hexanoic acid and phenylboronic acid in the presence of $[\mathrm{Pd(PPh_3)_4}]$ at 80 °C in dioxane (Table 3). Acetic anhydride was much less effective than pivalic anhydride as the activator (Run 2). We found that dialkyl dicarbontes are better promoters of the catalytic reaction than pivalic anhydride. Di-*t*-butyl dicarbonate gave a reasonably high yield of ketone (Run 3), but dimethyl dicarbonate was found particularly suitable for the reaction, giving the ketone in 95% (Run 4). Use of dimethyl dicarbonate had the other advantage that use of a large excess was not necessary, as was the case with pivalic anhydride in the ketone synthesis. The amount of dimethyl dicarbonate could be reduced to 1.2 mol amt. per carboxylic acid without affecting the product yield (Run 5). Further decrease to equimolar ratio of the activator/carboxylic acid caused some drop in the ketone yield, giving 75% of the ketone (Run 6).

(d) Examination of Amounts of Catalysts. Next we probed the necessary amount of the catalyst required for cross-coupling reaction of heptanoic acid with phenylboronic acid in the presence of dimethyl dicarbonate (Table 4). An excellent

Table 4. Influence of the Amount of Catalyst on the Cross-Coupling Reaction of Heptanoic Acid with Phenylboronic Acid



$$C_6H_{13}COOH + PhB(OH)_2 \xrightarrow[\text{dioxane, } 80\,^\circ C,\ 24\ h]{[Pd(PPh_3)_4],\ (MeOCO)_2O} C_6H_{13}C(=O)Ph$$

Rum[a)]	Pd/$C_6H_{13}COOH$	$C_6H_{13}COPh$/%[b)]	TON[c)]
1	0.02	94	47
2	0.01	92	92
3	0.005	94	188
4	0.001	70	700

a) Typical conditions: a mixture containing hexanoic acid (1 mmol), phenylboronic acid (1.2 mmol), dimethyl dicarbonate (1.5 mmol), $[Pd(PPh_3)_4]$ (0.01–0.02 mmol), and dioxane (5 cm^3) was stirred in a Schlenk tube under argon at 80 °C for 24 h.

b) Determined by GC using $^nC_{14}H_{30}$ as an internal standard.

c) TON = Turn over number.

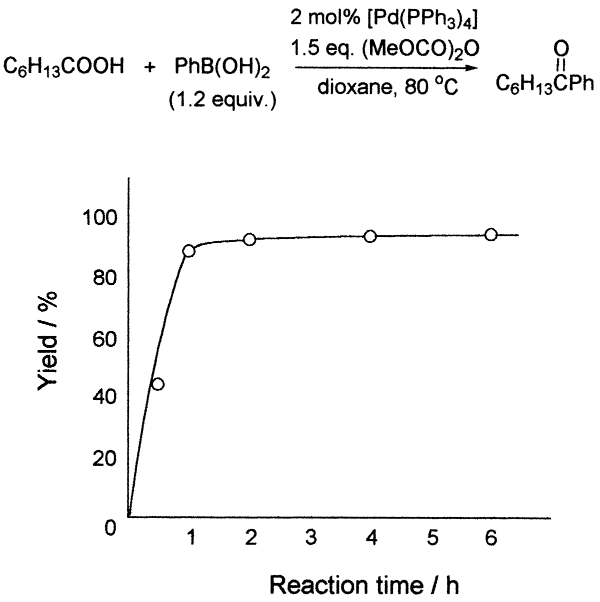


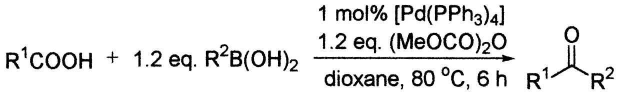
Fig. 1. Time course of the coupling reaction of $C_6H_{13}COOH$ with $PhB(OH)_2$ catalyzed by $[Pd(PPh_3)_4]$ carried out at 80 °C in dioxane in the presence of dimethyl dicarbonate.

yield of the ketone was obtained when the molar amount of $[Pd(PPh_3)_4]$ used per heptanoic acid was lowered to 0.005 (Run 3), but further decrease in the amount of $[Pd(PPh_3)_4]$ was found to give a lower yield of ketone (Run 4).

(e) Time Course. Figure 1 exhibits a typical time course in the reaction of heptanoic acid with phenylboronic acid in the presence of dimethyl dicarbonate in dioxane carried out at 80 °C. Use of $[Pd(PPh_3)_4]$ as a catalyst converted heptanoic acid into heptanophenone almost completely within 2 h, as shown in Fig. 1.

(f) Scope and Limitation. Table 5 summarizes representative examples of the palladium-catalyzed ketone synthesis from carboxylic acids and organoboronic acids in the presence of dimethyl dicarbonate. The present process is applicable to a large variety of substrates, including aromatic, heterocyclic, and aliphatic carboxylic acids, in combination with organoboron compounds, giving ketones in excellent yields. The process is tolerant of carboxylic acids having various functional groups. Benzoic acid derivatives having methoxy, methyl, formyl, trifluoromethyl, cyano, and nitro groups at the para positions can be catalytically converted into the corresponding ketones in excellent yields on treatment with arylboronic acids in the presence of dimethyl dicarbonate and $[Pd(PPh_3)_4]$ (Runs 2 – 10). *p*-Chlorobenzoic acid was transformed selectively into *p*-chlorobenzophenone without undergoing the C–Cl bond cleavage (Run 4).[26]

Table 5. Synthesis of Unsymmetrical Ketones by the Palladium-Catalyzed Cross-Coupling of Carboxylic Acids with Organoboronic Acids in the Presence of Dimethyl Dicarbonate



$$R^1COOH + 1.2\ eq.\ R^2B(OH)_2 \xrightarrow[\text{dioxane, } 80\,^\circ C,\ 6\ h]{1\ mol\%\ [Pd(PPh_3)_4],\ 1.2\ eq.\ (MeOCO)_2O} R^1C(=O)R^2$$

Entry[a)]	R^1	R^2	Yield/%[b)]
1	Ph	Ph	97
2	*p*-$MeOC_6H_4$	Ph	96 (86)
3	*p*-MeC_6H_4	Ph	97
4	*p*-ClC_6H_4	Ph	(88)
5	*p*-$F_3CC_6H_4$	Ph	(99)
6	*p*-$HCOC_6H_4$	*p*-MeC_6H_4	(88)
7	*p*-NCC_6H_4	Ph	98
8	*p*-$O_2NC_6H_4$	Ph	96
9	Ph	*p*-$MeOC_6H_4$	97
10	Ph	*p*-$F_3CC_6H_4$	98
11	*m*-MeC_6H_4	*m*-MeC_6H_4	(85)
12	3-furan	Ph	(85)
13	2-thiophene	Ph	99 (88)
14	3-pyridine	Ph	85
15	*trans*-PhCH=CH	Ph	56
16	Ph	*trans*-PhCH=CH	40
17	$^nC_6H_{13}$	Ph	96
18	^{i}Pr	Ph	52
19	^{t}Bu	Ph	20

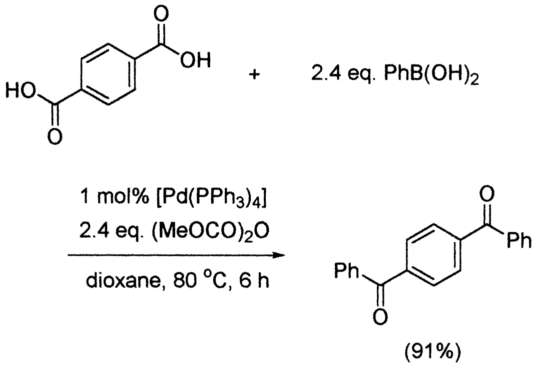
a) Typical conditions: a mixture containing carboxylic acid (1 mmol), organoboronic acid (1.2 mmol), dimethyl dicarbonate (1.2 mmol), $[Pd(PPh_3)_4]$ (0.01 mmol), and dioxane (5 cm^3) was stirred in a Schlenk tube under argon at 80 °C for 6 h. b) GC yields based on carboxylic acid. The isolated yields are in the parentheses.

Friedel–Crafts acylation generally displays ortho and para selectivity and is not suitable for preparation of aryl ketones with a meta substituent.[14] With the present method, on the other hand, 3, 3′-dimethyl benzophenone was selectively obtained in an excellent yield in the reaction of *m*-toluic acid and *m*-tolylboronic acid (Runs 11).

Heteroatoms which coordinate to transition metals often retard the cross-coupling reaction of organometallics. However, heterocyclic carboxylic acids such as 2-thiophenecarboxylic acid, 3-furoic acid, and nicotinic acid readily coupled with phenylboronic acid under standardized conditions to give the corresponding ketones in good yields (Runs 12 – 14). *trans*-Cinnamic acid having the double bond that may interact with the palladium center could be also used, although the yield was moderate (Run 15). The presence of C=C bond on the side of organoboronic acid also hinders preparation of ketones (Run 16).

Various aliphatic carboxylic acids such as heptanoic acid are converted smoothly into heptanophenone in combination with phenylboronic acid (Run 17), whereas a bulky aliphatic carboxylic acid such as 2, 2-dimethylpropionic acid and 2-methylpropionic acid resulted in low to moderate yields, probably due to the lower reactivity of their mixed anhydride in oxidative addition to a Pd(0) species (Runs 18 and 19).[27]

Aromatic and aliphatic dicarboxylic acids could also be converted into diketones in the catalytic process. As shown in Eqs. 7 and 8, terephthalic acid and azelaic acid were converted into the corresponding diketones in moderate to excellent yields on treatment with phenylboronic acid in the presence of dimethyl dicarbonate and $[Pd(PPh_3)_4]$.



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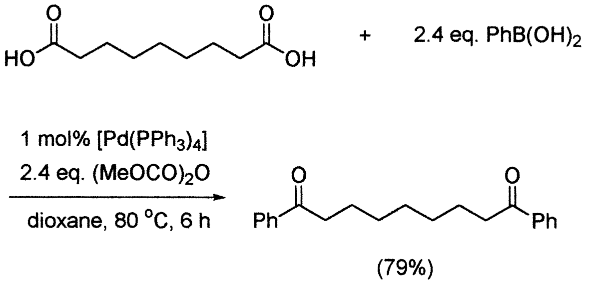
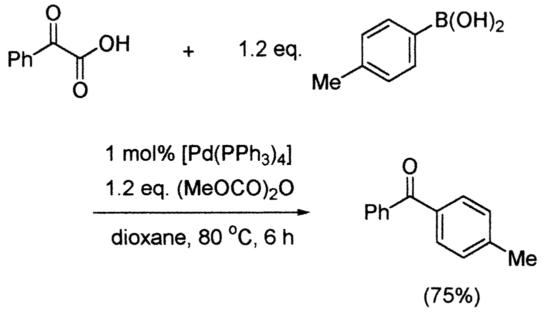


(8)

If the reaction could be applied to α-keto acids, we might find a new route to α-diketone synthesis. However, the reaction of benzoylformic acid with *p*-tolylboronic acid gave 4-methylbenzophenone as the major product without giving the expected α-diketone (Eq. 9). The result suggests that decarbonylation of the (phenylglyoxyl)palladium intermediate occurred to give a (benzoyl)palladium intermediate that further underwent transmetallation with *p*-tolylboronic acid to produce 4-methylbenzophenone.[28]

Organoboron compounds other than organoboronic acids were also examined. Employment of sodium tetraphenylborate[29] in a quantity somewhat higher than equimolar amount in combination with the benzoic acid gave benzophenone in 96% yield. A moderately high yield of benzophenone (72%) from benzoic acid was obtained even when 0.3 molar amount of $NaBPh_4$ per benzoic acid was employed in the presence of $[Pd(PPh_3)_4]$, the result indicating that three phenyl groups in $NaBPh_4$ were used in the transfer process. 2-Phenyl-1, 3, 2-dioxaborinane[30] was found less effective as the arylating reagents (Eq. 10).



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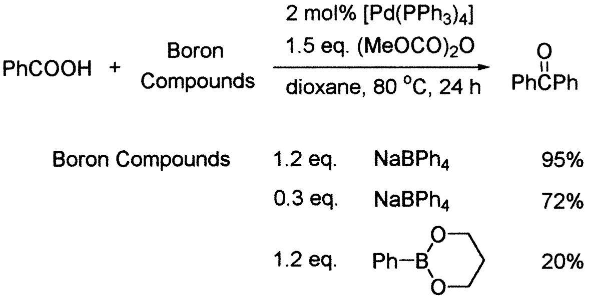


(10)

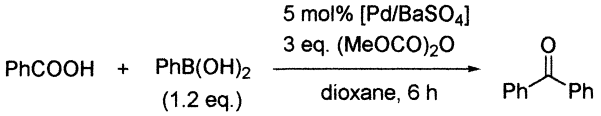
(g) Application to Heterogeneous Systems. Recently, the effect of addition of ligands not only to homogeneous catalyst systems but also to heterogeneous catalysts to control the reaction courses is attracting increasing attention.[31] Heterogeneous catalysts possess obvious advantages over the homogeneous systems in ease of separation of the catalysts and the product. The yield of ketone is influenced by nature and the amount of the phosphine ligands added to the heterogeneous catalysts. Development of the catalytic activity of the heterogeneous catalyst was favored at higher temperatures, as shown in Table 6.

The commercially available heterogeneous palladium catalysts such as palladium deposited on barium sulfate (unreduced samples) without added tertiary phosphine ligands did not catalyze the ketone synthesis (Run 1). Addition of triphenylphosphine to $Pd/BaSO_4$, however, developed the catalytic activities (Runs 2–13). Reactions carried out at 90 °C and under reflux conditions in dioxane afforded benzophenone in good yields (Runs 3 and 4), whereas the reaction carried out at 70 °C gave a lower yield (Run 2). A less polar solvent such as toluene was also found effective (Run 5). Among the tertiary phosphine ligands examined, triphenylphosphine gave the highest yields. Use of more electron-rich tertiary phosphine ligands than PPh_3 such as tris(*p*-methoxyphenyl)phosphine or less electron-rich ligands like tri-2-furylphosphine resulted in decrease in the yield of the ketone (Runs 6 and 7). The amount of PPh_3 contained in the catalytic systems also affected the catalytic activity. Addition of PPh_3 up to 4 mol amt./palladium caused improvement in the yield of the ketone, whereas further increase in the amounts of the ligand added showed an adverse effect (Runs 8–13).

Discussion

Reaction Mechanism. On the basis of our fundamental studies on the C–O bond cleavage of carboxylic anhydrides with Pd(0) complexes and further information on reactivity of an isolated acylpalladium complex with organoboronic acid,[7]

Table 6. Effect of Heterogeneous Catalysts on the Cross-Coupling Reaction of Benzoic Acid with Phenylboronic Acid in the Presence of $(MeOCO)_2O$

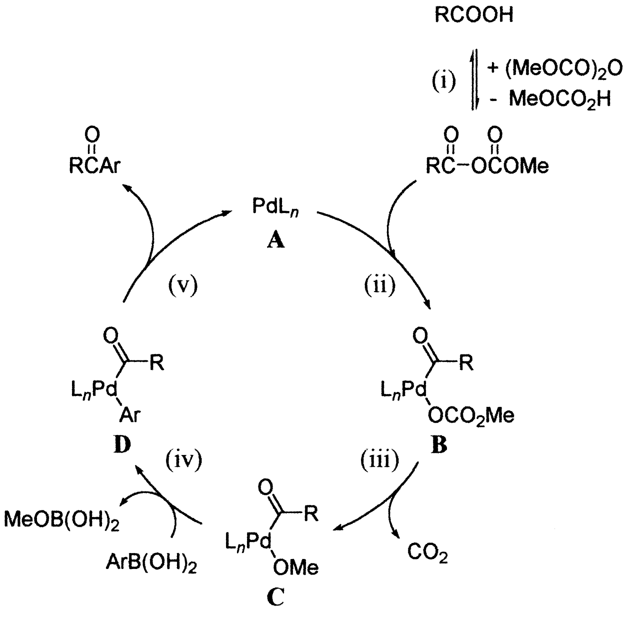


Rum[a]	Ligand	Temp	Yield/%[b]
1	None	90	trace
2	15 mol% PPh_3	70	52
3	15 mol% PPh_3	90	82
4	15 mol% PPh_3	reflux	80
5[c]	15 mol% PPh_3	90	81
6	15 mol% P (2-furyl)$_3$	90	20
7	15 mol% P (p-$MeOC_6H_4$)$_3$	90	52
8	5 mol% PPh_3	90	65
9	10 mol% PPh_3	90	76
10	20 mol% PPh_3	90	88
11	25 mol% PPh_3	90	81
12	30 mol% PPh_3	90	77
13	35 mol% PPh_3	90	49

a) Typical conditions: a mixture containing benzoic acid (1 mmol), phenylboronic acid (1.2 mmol), dimethyl dicarbonate (3.0 mmol), $[Pd/BaSO_4]$ (0.05 mmol), ligand, and dioxane (5 cm^3) was stirred in a Schlenk tube under argon at 80 °C for 6 h.

b) Determined by GC using $^{n}C_{14}H_{30}$ as an internal standard.

c) In toluene.

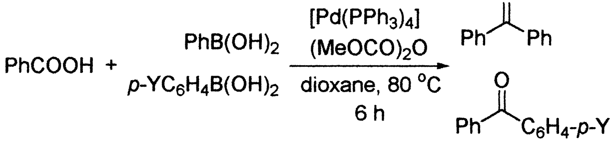


Scheme 3. Proposed mechanism for catalytic conversion of carboxylic acids into unsymmetrical ketones in the presense of dimethyl dicarbonatate.

we propose a catalytic cycle that consists of elementary processes as shown in Scheme 3 to account for the catalytic formation of aryl ketones from carboxylic acids and arylboronic acids in the presence of dimethyl dicarbonate.

The catalytic system includes: i) exchange reaction of the carboxylic acid employed with dimethyl dicarbonate added as the activator to form a mixed anhydride of the carboxylic acid and mono methyl ester of carbonic acid; ii) oxidative addition of the mixed anhydride to zerovalent palladium species **A** to give an (acyl)(methyl carbonato)palladium species **B**; iii) decarboxylation of the methyl carbonato ligand to give (acyl)(methoxo)palladium species **C**;[32] iv) transmetallation of **C** with an arylboronic acid to give an (acyl)(aryl)palladium species **D**; and v) reductive elimination of **D** to liberate the coupling product of the acyl and aryl ligands with regeneration of the Pd(0) species, which further carries the catalytic cycle.

Table 7. Reactivity of p-Substituted Phenylboronic Acids Relative to Phenylboronic Acid and Their Hammett Substituent Values



Y	Hammettσ_p	P(Y)/P(H)[a]	log (P(Y)/P(H))
Meo	−0.27	0.62	−0.21
Me	−0.17	0.72	−0.14
H	0	1	0
Cl	0.23	2.0	0.30
CF_3	0.54	2.1	0.32

a) Determined by GC using $^{n}C_{14}H_{30}$ as an internal standard.

For gaining further information on the mechanism of the present process, we carried out competition reactions using equimolar mixtures of phenylboronic acid and various para-substituted phenylboronic acids in the catalytic reactions with benzoic acid in the presence of dimethyl dicarbonate and $[Pd(PPh_3)_4]$. In Table 7 are compared relative product yields, P(Y)/P(H) of the ketones having the Y substituents at the para position versus benzophenone, produced after heating the systems for 6 h in dioxane at 80 °C. The results indicate that the para-substituted phenylboronic acids having the more electron-withdrawing substituents react faster than the phenylboronic acid derivatives having more electron-releasing substituents.[33]

Figure 2 demonstrates the results of the competition experiments using the four pairs of para-substituted phenylboronic acids and phenylboronic acid in the cross-coupling reactions with benzoic acid carried out at 80 °C in the presence of dimethyl dicarbonate and $[Pd(PPh_3)_4]$ as the catalyst. The plot of logarithms of the relative yields of the ketones against Hammett σ_p constants showed a reasonably good linear relationship ($r^2 = 0.904$) with a ρ value of 0.72. The positive ρ value suggests that the cross-coupling reaction is favored when the arylboronic acid has a higher Lewis acid character in the transmetallation process.

In the previous report dealing with palladium-catalyzed ketone synthesis from carboxylic anhydrides and arylboronic acids,[7] we observed that carboxylic anhydrides having electron-withdrawing para substituents in the benzoic anhydride reacted faster than the substrates having electron-donating substituents when phenylboronic acid was used as the arylation reagent in giving the aryl phenyl ketones. The result suggested the im-

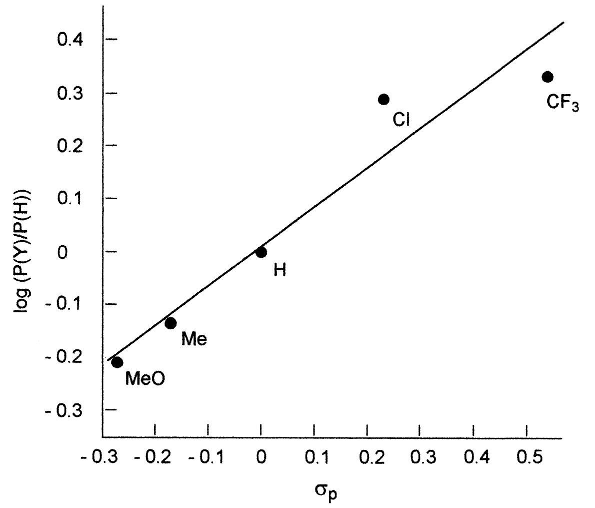


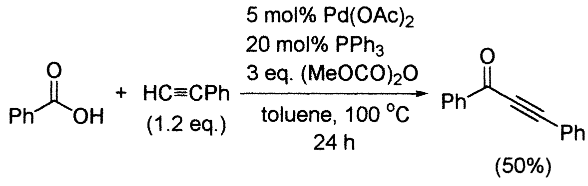
Fig. 2. Hammett plot for the relative reactivities of various para-substituted phenylboronic acids to phenylboronic acid in the cross-coupling reaction

portance of the oxidative addition of carboxylic anhydride in the catalytic cycle. Now that factors controlling the oxidative addition process (ii) in Scheme 3 and the transmetallation process (iv) in Scheme 3 have been clarified to some extent, examination of the factors involved in each of the elementary processes in Scheme 3 merits further studies in elucidating the reaction mechanism.

In the Suzuki–Miyaura coupling of organic halides or organic triflates with aryl-, alkenyl-, and alkylboronic acids or esters, addition of a base such as NaOEt, KOAc, and NaOH is required to drive the reactions.[17] The effect of addition of the base was accounted for as replacement of the halide ligand in the catalyst intermediate with the alkoxide, carboxylate, or hydroxide ligand that is more susceptible to transmetallation with the oxophilic organoboron compounds than a halide ligand.[34] In the present case, on the other hand, no base is required in performing the cross-coupling process to yield ketones.[35] The reason may be found in the reaction mechanism as represented by Scheme 3. If the mechanism shown in Scheme 3 is valid, the acyl(methoxo)palladium intermediate **C** produced by decarboxylation of **B** possesses the oxygen-containing methoxide ligand amenable to the attack of the oxophilic arylboronic acid to give **D** in step (iv) in Scheme 3.

Catalytic Synthesis of Alkynyl Ketone. On the basis of the present study that supports involvement of the acyl(methoxo)palladium complexes generated in the reaction mixture of carboxylic acids with dimethyl dicarbonate on reaction with Pd(0) complex, we further examined the possibility of developing a catalytic process to cause the coupling of the acyl entity in the carboxylic acid with terminal alkynes. It was found that the benzoic acid was converted into 1,3-diphenyl-2-propyn-1-one[36] when it was treated with dimethyl dicarbonate and phenylacetylene in the presence of $Pd(OAc)_2$ and PPh_3 as shown in Eq. 11.

The catalytic coupling reaction is considered to proceed through oxidative addition of the mixed anhydride produced from benzoic acid and dimethyl dicarbonate to give the acylpalladium intermediate **B**, as shown in Scheme 3. The acylpalladium complex **B** further undergoes decarboxylation, deprotonation of phenylacetylene by the methoxide, and coupling of the acyl entity with the phenylethynyl entity, producing the product and the catalyst. Applicability of the present methodology for synthesis of alkynyl ketones will be the subject of further studies.



(11)

While we were preparing this paper, Gooβen et al. have reported a similar synthetic method of ketones from carboxylic acids with organoboronic acids in the presence of pivalic anhydride.[37] They used a concept similar to ours reported in our previous study on the aldehyde synthesis.[9] However, as we described in the present paper, the cross-coupling process using pivalic anhydride as an activator is less satisfactory than the present method with dimethyl dicarbonate in view of the somewhat lower yields in giving ketones and in view of the higher cost of pivalic anhydride than of dimethyl dicarbonate. More recently, they reported also on the Pd-catalyzed cross-coupling reaction of carboxylic acids with arylboronic acids in the presence of disuccinimido carbonate as the activator.[38] However, in the coupling reaction using disuccinimido carbonate as the activator, addition of a base such as sodium carbonate is necessary to drive the reaction. In addition, disuccinimido carbonate is more expensive than dimethyl dicarbonate.

Conclusion

We demonstrated here a new type of catalytic process to convert carboxylic acids and organoboron compounds into unsymmetrical ketones in one-pot under mild and neutral conditions. The present process is applicable to various carboxylic acids and organoboron compounds and is tolerant of a variety of functional groups, such as cyano, nitro, and carbonyl groups, and does not cause the C–Cl bond cleavage. Many kinds of heterocyclic carboxylic acids can be readily coupled with arylboronic acids under mild experimental conditions. The present method allows the use of an α, β-unsaturated carboxylic acid such as *trans*-cinnamic acid. Dibasic carboxylic acids could be also used to give diketones. Our studies of competition reactions showed that arylboronic acids having electron-withdrawing para substituents reacted faster, the result suggesting the importance of the electrophilicity of the arylboronic acid in transmetallation process.

In view of the paucity of atom-efficient and environmentally benign processes to synthesize unsymmetrical ketones under mild conditions, the present method provides a convenient new route to selective production of ketones under mild conditions. We also found that a direct catalytic conversion of benzoic acid with phenylacetylene into 1,3-diphenyl-2-propyn-1-one can be achieved under similar conditions.

Experimental

General Procedures. All manipulations were carried out under argon atmosphere using Schlenk tube techniques. Solvents were purified by the usual methods under argon. NMR spectra were recorded on a JEOL Lambda 500 or a JEOL AL-400 spectrometer for ^{1}H (referenced via residual solvent protons), ^{13}C{^{1}H} (referenced to the solvent resonance), and ^{19}F (referenced to trifluoroacetic acid in $CDCl_3$ as an external standard) NMR. Coupling constants (J values) are given in hertz (Hz), and spin multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), vt (virtual triplet), and br (broad). Gas chromatographic analyses (GC) were carried out on a GC-353 equipped with TC1 column (0.25 mm i. d. × 30 m), using N_2 as carrier gas. Low-resolution mass spectra were obtained with a JEOL JMS-Automass 150 that is coupled with a gas chromatograph. FAB analysis was performed by the Materials Characterization Central Laboratory of Waseda University.

Reagents. All carboxylic acids, carboxylic anhydrides, organoboron compounds, and di-*t*-butyl dicarbonate were commercial products and were used without further purification. Dimethyl dicarbonate purchased from Aldrich was distilled before use. Phenylacetylene was a commercial product, and was used directly. $[Pd(PPh_3)_4]$[39] and $[Pd(PCy_3)_2]$[40] were prepared by the reported procedures. $[Pd_2(dba)_3]$ was prepared following a synthesis report[41] and was used without recrystallization of the crude precipitate obtained at the end of the synthesis. $Pd(OAc)_2$ (Aldrich) and $Pd/BaSO_4$/(unreduced) (Aldrich) were used as received from commercial suppliers. All tertiary phosphines were commercial products and were used without further purification.

Effect of Homogeneous Catalysts (Table 1). A typical procedure is as follows (Run 2). A dioxane solution (5 cm^3) containing $[Pd(PCy_3)_2]$ (33.4 mg, 0.0501 mmol), *p*-toluic acid (136 mg, 0.999 mmol), phenylboronic acid (147 mg, 1.21 mmol), and pivalic anhydride (560 mg, 3.01 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 24 h. The yields of 4-methylbenzophenone were determined by GC using *n*-tetradecane ($^nC_{14}H_{30}$) as an internal standard.

Effects of Solvent and Temperature (Table 2). A typical procedure is as follows (Run 4). Dioxane solutions (5 cm^3) containing $[Pd(PPh_3)_4]$ (58.0 mg, 0.0502 mmol), *p*-toluic acid (139 mg, 1.02 mmol), phenylboronic acid (147 mg, 1.21 mmol), and pivalic anhydride (560 mg, 3.01 mmol) in a 25 cm^3 Schlenk tube were stirred under argon at room temperature at 60 °C, 80 °C, and 100 °C, respectively, for 24 hours. The effects of solvents were examined in THF, acetone, toluene, 1-methyl-2-pyrrolidinone (NMP), hexane, and dioxane by carrying out the syntheses at 80 °C. The yields of 4-methylbenzophenone were determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Effect of Activator (Table 3). A typical procedure is as follows (Run 4). A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (23.1 mg, 0.0200 mmol), heptanoic acid (129 mg, 0.991 mmol), phenylboronic acid (148 mg, 1.21 mmol), and dimethyl dicarbonate (400 mg, 2.98 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 24 h. The yields of heptanophenone were determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Influence of the Amount of Catalyst (Table 4). A typical procedure is as follows (Run 2). A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (11.6 mg, 0.0100 mmol), heptanoic acid (129 mg, 0.991 mmol), phenylboronic acid (146 mg, 1.20 mmol), and dimethyl dicarbonate (200 mg, 1.49 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 24 h. The yields of heptanophenone were determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Time-Yield Curve in Formation of Heptanophenone (Fig. 1). A procedure for obtaining the time-yield curve in synthesis of heptanophenone is as follows. A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (23.1 mg, 0.0200 mmol), heptanoic acid (129 mg, 0.991 mmol), phenylboronic acid (147 mg, 1.21 mmol), and dimethyl dicarbonate (200 mg, 1.49 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C. At each interval, the tube was removed from the oil bath and cooled in a water bath immediately. The yields of heptanophenone were determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Synthesis of Unsymmetrical Ketones (Table 5). A typical procedure is as follows (Run 5). A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (11.9 mg, 0.0103 mmol), 4-trifluoromethylbenzoic acid (191 mg, 1.00 mmol), phenylboronic acid (147 mg, 1.21 mmol), and dimethyl dicarbonate (164 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for six hours. On cooling the reaction mixture, diethyl ether and H_2O were added and the aqueous layer was extracted with diethyl ether. The combined ether solution was dried ($MgSO_4$) and the solvent was evaporated in vacuo. Purification of the residue by column chromatography (hexane/ethyl acetate = 9:1) gave the corresponding product (249 mg; yield 99%).

The following ketones were synthesized by the above general procedure. GC yields based on carboxylic acids are in the parenthesis. The isolated yields are indicated by the square brackets.

Benzophenone (Run 1): [119-61-9] (97%); Benzophenone was characterized by GC-MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC-MS *m*/*z* (rel intensity) 182 (100), 105 (54), 77 (66).

4-Methoxybenzophenone (Run 2): [611-64-9] (96%) [86%]; 4-Methoxybenzophene was characterized by ^{1}H, ^{13}C{^{1}H} NMR, and GC-MS by comparison with an authentic sample (Aldrich). ^{1}H NMR (acetone-d_6, r. t., 400 MHz) δ 7.67 (m, 2H, aromatic H), 7.61 (m, 2H, aromatic H), 7.49 (m, 1H, aromatic H), 7.41 (m, 2H, aromatic H), 6.95 (m, 2H, aromatic H), 3.79 (s, OCH_3); ^{13}C{^{1}H} NMR (acetone-d_6, r. t., 100 MHz) δ 195.0 (s, carbonyl C), 164.1 (s, aromatic C), 139.1 (s, aromatic C), 132.9 (s, aromatic C), 132.5 (s, aromatic C), 130.8 (s, aromatic C), 130.1(s, aromatic C), 129.0 (s, aromatic C), 114.4 (s, aromatic C), 55.9 (s, OCH_3). GC–MS *m*/*z* (rel intensity) 212 (42), 135 (98), 105 (13), 92 (14), 77 (46).

4-Methylbenzophenone (Run 3): [634-65-2] (97%); 4-Methylbenzophene was characterized by GC-MS by comparison with an authentic sample (Kanto Chemical Co.). GC-MS *m*/*z* (rel intensity) 196 (99), 181 (21), 165 (9), 152 (8), 119 (95), 105 (50), 91 (68), 77 (74).

4-Chlorobenzophenone (Run 4): [134-85-0] [88%]; 4-Chlorobenzophenone was characterized by ^{1}H, ^{13}C{^{1}H} NMR, and GC-MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). ^{1}H NMR (acetone-d_6, r. t., 400 MHz) δ 7.69–7.65 (m, 4H, aromatic H), 7.57–7.53 (m, 1H, aromatic H), 7.49–7.42 (m, 4H, aromatic H); ^{13}C{^{1}H} NMR (acetone-d_6, r. t., 100 MHz) δ 195.2 (s, carbonyl C), 138.8 (s, aromatic C), 138.0 (s, aromatic C), 137.0 (s, aromatic C), 133.3 (s, aromatic C), 132.2 (s. aromatic C), 130.4 (s, aromatic C), 129.3 (s, aromatic C), 129.2 (s, aromatic C). GC-MS *m*/*z* (rel intensity) 216 (9), 181 (3), 152 (2), 139 (29), 111 (42), 105 (73), 77 (100).

4-Trifluoromethylbenzophenone (Run 5): [728-86-9] [98%]; 4-Trifluoromethybenzophenone was characterized by ^{1}H, ^{13}C{^{1}H} NMR, and GC-MS by comparison with an authentic sample (ACROS). ^{1}H NMR (acetone-d_6, r. t., 400 MHz) δ 7.84 (m, 2H, aromatic H), 7.79 (m, 2H, aromatic H), 7.71–7.69 (m, 2H, aromatic

H), 7.58–7.56 (m, 1H, aromatic H), 7.47–7.44 (m, 2H, aromatic H); ^{13}C{^{1}H} NMR ($CDCl_3$, r. t., 100 MHz) δ 195.3 (s, carbonyl C), 146.6 (s, aromatic C), 136.6 (s, aromatic C), 133.6 (q, $^{2}J_{CF}$ = 32.3 Hz aromatic C), 133.0 (s, aromatic C), 130.0 (s, aromatic C), 130.0 (s, aromatic C), 128.4 (s, aromatic C), 125.3 (q, $^{3}J_{CF}$ = 3.32 Hz aromatic C), 123.6 (q, $^{1}J_{CF}$ = 272.0 Hz, *C*F$_3$); ^{19}F NMR (acetone-*d*$_6$, r. t., 471 MHz) δ −62.2 (s, C*F*$_3$). GC–MS *m*/*z* (rel intensity) 250 (52), 231 (7), 173 (47), 145 (52), 125 (9), 105 (96), 77 (99).

4-Formyl-4′-methylbenzophenone (Run 6): [88%]; ^{1}H NMR ($CDCl_3$, r. t., 400 MHz) δ 10.13 (s, 1H, formyl H), 8.00 (m, 2H, aromatic H), 7.90 (m, 2H, aromatic H), 7.72 (m, 2H, aromatic H), 7.31 (m, 2H, aromatic H), 2.46 (s, 3H, C*H*$_3$); ^{13}C{^{1}H} NMR ($CDCl_3$, r. t., 100 MHz) δ 195.4 (carbonyl C), 191.5 (formyl C), 144.1 (s, aromatic C), 142.9 (s, aromatic C), 138.2 (s, aromatic C), 134.0 (s, aromatic C), 130.3 (s, aromatic C), 130.1 (s, aromatic C), 129.4 (s, aromatic C), 129.2 (s, aromatic C), 21.8 (s, *C*H$_3$). GC–MS *m*/*z* (rel intensity) 224 (26), 195 (5), 165 (6), 152 (5), 133 (11), 119 (98), 104 (10), 91 (43), 77 (23). FAB-MS: Found *m*/*z* 225.0902 (M + H), Calcd for $C_{15}H_{12}O_2$: 224.0837 (M).

4-Cyanobenzophenone (Run 7): [1503-49-7] (98%); 4-Cyanobenzophenone was characterized by GC–MS by comparison with an authentic sample (Aldrich). GC–MS *m*/*z* (rel intensity) 207 (42), 130 (26), 105 (99), 77 (55).

4-Nitrobenzophenone (Run 8): [1144-74-4] (96%); 4-Nitrobenzophene was characterized by GC–MS by comparison with an authentic sample (Aldrich). GC–MS *m*/*z* (rel intensity) 227 (32), 207 (6), 150 (12), 105 (100), 77 (55).

4-Methoxybenzophenone (Run 9): [611-64-9] (97%); 4-Methoxybenzophene was characterized by GC–MS by comparison with an authentic sample (Aldrich). GC–MS *m*/*z* (rel intensity) 212 (42), 135 (98), 105 (13), 92 (14), 77 (46).

4-Trifluoromethylbenzophenone (Run 10): [728-86-9] (98%); 4-Trifluoromethybenzophenone was characterized by GC–MS by comparison with an authentic sample (ACROS) . GC–MS *m*/*z* (rel intensity) 250 (87), 231 (7), 173 (52), 145 (73), 125 (13), 105 (98), 77 (99).

3, 3′-Dimethylbenzophenone (Run 11): [2852-68-8] [85%]; 3, 3′-Dimethylbenzophenone was characterized by ^{1}H and ^{13}C{^{1}H} NMR by comparison with the literature.[42] ^{1}H NMR ($CDCl_3$, r. t., 400 MHz) δ 7.62 (s, 2H, aromatic H), 7.56 (m, 2H, aromatic H), 7.40–7.35 (m, 4H, aromatic H), 2.41 (s, 6H, C*H*$_3$); ^{13}C{^{1}H} NMR ($CDCl_3$, r. t., 100 MHz) δ 197.0 (s, carbonyl C), 138.0 (s, aromatic C), 137.7 (s, aromatic C), 133.0 (s, aromatic C), 130.3 (s, aromatic C), 127.9 (s, aromatic C), 127.2 (s, aromatic C), 21.4 (s, *C*H$_3$). GC–MS *m*/*z* (rel intensity) 210 (23), 195 (14), 165 (6), 119 (99), 91 (50).

3-Benzoylfuran (Run 12): [6453-98-1] [85%]; 3-Benzoylfuran was characterized by ^{1}H and ^{13}C{^{1}H} NMR by comparison with the literature.[43] ^{1}H NMR (acetone-*d*$_6$, r. t., 400 MHz) δ 8.19 (s, 1H, aromatic H), 7.88 (m, 2H, aromatic H), 7.73 (s, 1H, aromatic H), 7.64 (m, 1H, aromatic H), 7.53 (m, 2H, aromatic H), 6.90 (s, 1H, aromatic H); ^{13}C{^{1}H} NMR ($CDCl_3$, r. t., 100 MHz) δ 189.2 (s, carbonyl C), 148.4 (s, aromatic C), 143.8 (s, aromatic C), 138.7 (s, aromatic C), 132.4 (s, aromatic C), 128.7 (s, aromatic C), 128.4 (s, aromatic C), 126.4 (s, aromatic C), 110.1 (s, aromatic C). GC–MS *m*/*z* (rel intensity) 172 (78), 144 (9), 115 (20), 105 (24), 95 (99), 77 (63).

2-Benzoylthiophene (Run 13): [135-00-2] (99%) [88%]; 2-Benzoylthiophene was characterized by ^{1}H, ^{13}C{^{1}H} NMR, and GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). ^{1}H NMR (acetone-*d*$_6$, r. t., 400 MHz) δ 7.98 (m, 2H, aromatic H), 7.86 (m, 1H, aromatic H), 7.71 (m, 1H, aromatic H), 7.66 (m, 1H, aromatic H), 7.55 (m, 2H, aromatic H), 7.26 (m, 1H aromatic H); ^{13}C{^{1}H} NMR (acetone-*d*$_6$, r. t., 100 MHz) δ 187.9 (s, carbonyl C), 144.2 (s, aromatic C), 138.9 (s, aromatic C), 135.6 (s, aromatic C), 135.2 (s, aromatic C), 132.9 (s, aromatic C), 129.6 (s, aromatic C), 129.2 (s, aromatic C), 129.0 (s, aromatic C). GC–MS *m*/*z* (rel intensity) 188 (99), 171 (13), 160 (12), 111 (97), 105 (72), 77 (98).

3-Benzoylpyridine (Run 14): [5424-19-1] (85%); 3-Benzoylpryridine was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 183 (80), 154 (6), 105 (89), 77 (99).

Chalcone (Run 15): [614-47-1] (56%); Chalcone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 208 (47), 179 (15), 165 (9), 131 (29), 105 (23), 77 (100).

Chalcone (Run 16): [614-47-1] (43%); Chalcone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 208 (50), 179 (16), 165 (9), 131 (30), 105 (23), 77 (100).

Heptanophenone (Run 17): [1671-75-6] (96%); Heptanophenone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 190 (44), 133 (40), 120 (82), 105 (72), 91 (11), 77 (100).

Isobutyrophenone (Run 18): [611-70-1] (52%); Isobutyrophenone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 148 (17), 105 (99), 77 (49).

2, 2-Dimethylpropiophenone (Run 19): [938-16-9] (20%); 2,2-Dimethylpropiophenone was characterized by GC–MS by comparison with an authentic sample (Aldrich). GC–MS *m*/*z* (rel intensity) 162 (23), 119 (6), 105 (97), 91 (7), 77 (100).

Cross-Coupling Reaction of Dibasic Carboxylic Acids (Eqs. 7 and 8). A typical procedure is as follows (Eq. 8). A dioxane solution (5 cm^3) containing [Pd(PPh$_3$)$_4$] (12.1 mg, 0.0105 mmol), azelaic acid (188 mg, 0.999 mmol), phenylboronic acid (293 mg, 2.40 mmol), and dimethyl dicarbonate (325 mg, 2.42 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for six hours. After the reaction mixture was cooled, diethyl ether and H_2O were added and the aqueous layer was extracted with diethyl ether. The combined ether solution was dried ($MgSO_4$) and the solvent was evaporated in vacuo. Purification of the residue by column chromatography (hexane/ethyl acetate = 9:1) gave the corresponding product (245 mg; yield 79%).

1, 9-Diphenyl-1, 9-nonanedione (Eq. 8): [28861-21-4] (79%); 1,9-Diphenyl-1,9-nonanedione was characterized by ^{1}H NMR by comparison with the literature.[44] ^{1}H NMR ($CDCl_3$, r. t., 400 MHz) δ 7.88 (m, 4H, aromatic H), 7.48 (m, 2H, aromatic H), 7.38 (m, 4H, aromatic H), 2.90 (t, 4H, $^{3}J_{HH}$ = 7.45 Hz, COC*H*$_2$), 1.69–1.65 (m, 4H, alkyl H), 1.35–1.28 (m, 6H, alkyl H); ^{13}C{^{1}H} NMR ($CDCl_3$, r. t., 100 MHz) δ 200.3 (s, carbonyl C), 137.0 (s, aromatic C), 132.8 (s, aromatic C), 128.5 (s, aromatic C), 127.9 (s, aromatic C), 38.6 (s, CO*C*H$_2$), 29.4 (s, alkyl C), 29.2 (s, alkyl C), 24.3 (s, alkyl C).

1, 4-Dibenzoylbenzene (Eq. 7): [3016-97-5] (91%); 1, 4-Dibenzoylbenzene was characterized by GC–MS by comparison with an authentic sample (Aldrich). GC–MS *m*/*z* (rel intensity) 286 (30), 209 (38), 181 (12), 152 (19), 105 (100), 77 (87).

Cross-Coupling Reaction of Benzoylformic Acid (Eq. 9). A dioxane solution (5 cm^3) containing [Pd(PPh$_3$)$_4$] (11.9 mg, 0.0103 mmol), benzoylformic Acid (149 mg, 0.992 mmol), *p*-tolylboronic acid (165 mg, 1.21 mmol), and dimethyl dicarbonate (163 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 6 h. The yield of 4-methylbenzophenone was determined by GC using $^n C_{14}H_{30}$ as an internal standard. 4-Methylbenzophenone was characterized by GC–MS by comparison with an authentic sample (Kanto Chemical Co.). GC–MS *m*/*z* (rel intensity) 196 (42), 181 (13), 165 (5), 152 (5), 119 (96), 105 (25), 91 (39), 77 (45).

Cross-Coupling Reaction of Benzoic Acid with Other Organoboron Compounds in the Presence of Dimethyl Dicarbonate (Eq. 10). A typical procedure using $NaBPh_4$ is given below. A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (23.2 mg, 0.0201 mmol), benzoic acid (122 mg, 0.999 mmol), sodium tetraphenylborate (410 mg, 1.20 mmol), and dimethyl dicarbonate (200 mg, 1.49 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 24 h. The yields of benzophenone were determined by GC using $^n C_{14}H_{30}$ as an internal standard. Benzophenone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 182 (81), 105 (98), 77 (97).

Effect of Heterogeneous Catalysts (Table 6). A typical procedure is as follows (Run 10). A dioxane solution (5 cm^3) containing $Pd/BaSO_4$ (5 wt%) (106 mg, 0.0498 mmol), triphenylphosphine (54.0 mg, 0.206 mmol), benzoic acid (123 mg, 1.01 mmol), phenylboronic acid (146 mg, 1.20 mmol), and dimethyl dicarbonate (400 mg, 2.98 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 90 °C for 6 h. The yield of benzophenone was determined by GC using $^n C_{14}H_{30}$ as an internal standard. Benzophenone was characterized by GC–MS by comparison with an authentic sample (Tokyo Kasei Kogyo Co.). GC–MS *m*/*z* (rel intensity) 182 (100), 105 (97), 77 (98).

Competitive Reactions of Various Para-Substituted Phenylboronic Acids and Phenylboronic Acid (Table 7, Fig. 2). A typical procedure is as follows. A dioxane solution (5 cm^3) containing $[Pd(PPh_3)_4]$ (11.6 mg, 0.0100 mmol), benzoic acid (121 mg, 0.991 mmol), 4-methoxyphenylboronic acid (456 mg, 3.00 mmol), phenylboronic acid (367 mg, 3.01 mmol), and dimethyl dicarbonate (163 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 6 h. The GC analysis revealed that 52% of benzophenone and 32% of 4-methoxybenzophenone were generated in the reaction mixture. On the basis of the amounts of the two ketones, the relative reactivity of phenylboronic acids was determined as 0.62.

Cross-Coupling Reaction of Benzoic Acid with Phenylacetylene (Eq. 11). A toluene solution (5 cm^3) containing $Pd(OAc)_2$ (11.7 mg, 0.0521 mmol), triphenylphosphine (53.1 mg, 0.202 mmol), benzoic acid (123 mg, 1.01 mmol), phenylacetylene (121 mg, 1.18 mmol), and dimethyl dicarbonate (400 mg, 2.98 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 100 °C for 24 h. The yield of 1,3-diphenyl-2-propyn-1-one was determined by GC using $^n C_{14}H_{30}$ as an internal standard. 1, 3-Diphenyl-2-propyn-1-one [7338-94-5] was characterized by ^{1}H and $^{13}C\{^1H\}$ NMR by comparison with the literature.[36k] ^{1}H NMR ($CDCl_3$, r. t., 400 MHz) δ 8.22 (m, 2H, aromatic H), 7.69 (m, 2H, aromatic H), 7.62 (m, 1H, aromatic H), 7.52 (m, 2H, aromatic H), 7.48 (m, 1H, aromatic H), 7.42 (m, 2H, aromatic H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, r. t., 100 MHz) δ 177.8 (s, carbonyl C), 136.8 (s, aromatic C), 134.0 (s, aromatic C), 132.9 (s, aromatic C), 130.6 (s, aromatic C), 129.4 (s, aromatic C), 128.5 (s, aromatic C), 128.5 (s, aromatic C), 120.0 (s, aromatic C), 93.1 (s, alkyne), 86.8 (s, alkyne). GC–MS *m*/*z* (rel intensity) 206 (49), 178 (79), 129 (100), 77 (20).

This study was supported by grants from the Ministry of Education, Science, Sports and Culture and Nippon Zeon Co., Ltd. We are grateful for their support.

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