Preparation of 3(2*H*)-Furanones from 2-Propynyl Alcohol, CO, and Phenyl Halides under CO_2 Atmosphere Catalyzed by Transition Metal Complexes

Yoshio INOUE,* Kunihiro OHUCHI, I-Fang YEN, and Shin IMAIZUMI
Department of Engineering Science, Faculty of Engineering, Tohoku University, Aramaki, Aoba-ku, Sendai 980

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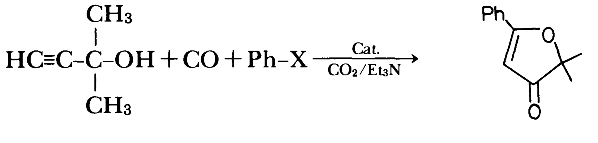
The novel synthetic method for 2,2-dimethyl-5-phenyl-3(2*H*)-furanone (bullatenone) from 2-methyl-3-butyn-2-ol, CO, and phenyl halides in the presence of a catalytic amount of transition metal complexes under the influence of CO_2 has been described. It was revealed that there was the intermediate formation of an acetylenic ketone from the acetylenic alcohol, CO, and the phenyl halide followed by the formation of a cyclic carbonate from the acetylenic ketone and CO_2 which underwent the decarboxylative transformation into the 3(2*H*)-furanone quantitatively.

In recent years, considerable interest has been paid for the fixation of carbon dioxide (CO_2) from the points of the recycle of carbon resources and the environment.[1)]

During the course of our studies directed at the effective utilization of CO_2, we have explored that 2-methyl-3-butyn-2-ol (**1**) reacts with carbon monoxide (CO) and phenyl halides in the presence of a catalytic amount of transition metal complexes to afford 2,2-dimethyl-5-phenyl-3(2*H*)-furanone (**2a**) under the influence of CO_2.[2)]



1 **2a**

The product **2a** is called bullatenone, which occurs in the essential oil of Myrtus bullata, a shrub endemic to New Zealand.[3)] The 3(2*H*)-furanone ring is contained in many naturally occurring compounds characterized by important biological activity as antitumor agents (eremantholides, geiparvarin) or aroma constituents.[4)]

It appears that the straightforward production of the furanone from the starting materials is difficult. Furthermore the role of CO_2 on this reaction is not distinct, partly because it does not enter into the stoichiometry. In this paper we describe the elucidation of the reaction pathway as well as the scope of this new method for the synthesis of 3(2*H*)-furanones.

Results and Discussion

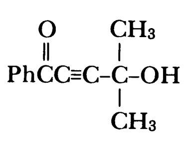
Various Group 8, 9, and 10 transition metal–triphenylphosphine complexes were active as the catalyst for the formation of the furanone **2a** from the acetylenic alcohol **1**, CO, and iodobenzene in triethylamine under the influence of CO_2 as shown in Table 1. Yields, in general, were moderate to reasonable except in the case of [$RhCl(PPh_3)_3$], where the yield was only modest. In the present reaction triethylamine functions as a base as well as a solvent. The employment of Na_2CO_3 or K_2CO_3 as the base resulted in the marked decrease in the yield. The effect of CO_2 was significant since the yield of **2a** dropped considerably and oily products came out when the reaction was performed under CO atmosphere.

Table 1. Effect of Catalyst on the Synthesis of **2a**[a)]

Catalyst	Solvent	Base	Yield of **2a**[b)]/%
$FeCl_2(PPh_3)_2$	NEt_3	—	62 (21)
$CoCl_2(PPh_3)_2$	NEt_3	—	61 (29)
$CoCl_2(PPh_3)_2$	CH_3CN	K_2CO_3	15
$NiCl_2(PPh_3)_2$	NEt_3	—	57 (36)
$RuCl_2(PPh_3)_3$	NEt_3	—	52 (19)
$RhCl(PPh_3)_3$	NEt_3	—	18 (3)
$PdCl_2(PPh_3)_2$	NEt_3	—	48 (38)
$PdCl_2(PPh_3)_2$	DMF	Na_2CO_3	18
$PdCl_2(PPh_3)_2$	CH_3CN	K_2CO_3	20
$PdCl_2(PPh_3)_2$	CH_3CN	Li_2CO_3	Trace
$PdCl_2(PPh_3)_2$	CH_3CN	Et_3N	69
$Pd(PPh_3)_3$	NEt_3	—	79 (26)
$Pd(PPh_3)_3$	Toluene	Na_2CO_3	0
$Pd(PPh_3)_4$	NEt_3	—	45 (40)
$Pd(PPh_3)_4$	CH_3CN	K_2CO_3	8
$PtCl_2(PPh_3)_2$	NEt_3	—	45 (23)
$Pt(PPh_3)_4$	NEt_3	—	64 (35)

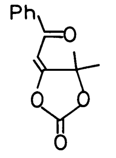
a) **1** 10 mmol, PhI 10 mmol, CO 10 atm, CO_2 10 atm, catalyst 0.2 mmol, solvent 10 cm^3, base 15 mmol; 100 °C, 8 h. b) GLC yield. The figures in the parentheses represent the yields of the reactions performed under CO atmosphere.

In order to elucidate the reaction pathway as well as the role of CO_2, the reaction was performed at 100 °C under CO atmosphere using [$PdCl_2(PPh_3)_2$] as the catalyst. With a shorter reaction time rather than the standard 8 h reaction, an acetylenic ketone, 4-hydroxy-4-methyl-1-phenyl-2-pentyn-1-one (**3**) was formed as the major product. As shown in Fig. 1, the acetylenic ketone **3** occurred at the early stage and decreased gradually, while the furanone **2a** was generated slowly and almost linearly. The acetylenic ketone appears to be an intermediate for the furanone formation. Apparently, however, not all the acetylenic ketone **3** produced was converted into **2a**. This observation is consistent with the production of the oily substance (vide supra).



$$\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{C{\equiv}C{-}}\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{{-}OH}$$

3



4

On the other hand (*E*)-4-benzoylmethylene-5,5-dimethyl-1,3-dioxolan-2-one (**4**) was produced at the early stage of the reaction in the presence of both CO and CO_2 with $[PdCl_2(PPh_3)_2]$ as the catalyst (Fig. 2). The formation of the acetylenic ketone **3** was not observed in this case. It seems interesting that both CO and CO_2 are incorporated in one molecule. The cyclic carbonate **4** decreased fairly rapidly with efficient formation of the furanone **2a** under the reaction conditions. Consequently the carbonate **4** seems to be another intermediate. This was confirmed actually as follows. The carbonate **4** was subjected to the thermal degradation at 100 °C for 1 h in the presence of 2 molar % of $[Pd(PPh_3)_4]$ under either CO or CO_2 atmosphere. This process led to 73 and 75% conversion of **4** into the furanone **2a**, respectively. The degradation of **4** at 150 °C for 20 min led to the complete conversion into the furanone **2a** after the quantitative evolution of CO_2.

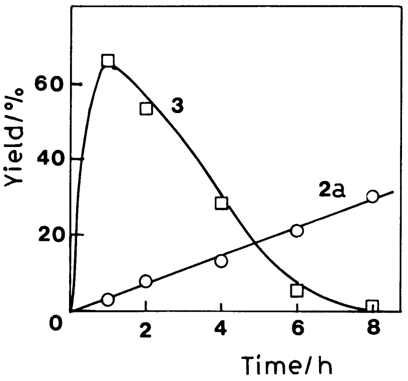


Fig. 1. Reaction of **1** with PhI under CO atmosphere with a $[PdCl_2(PPh_3)_2]$ catalyst.

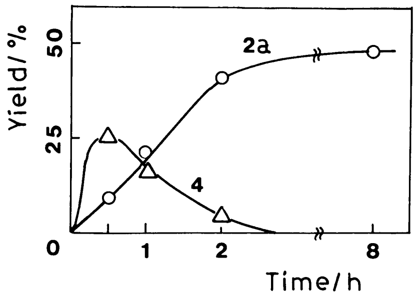
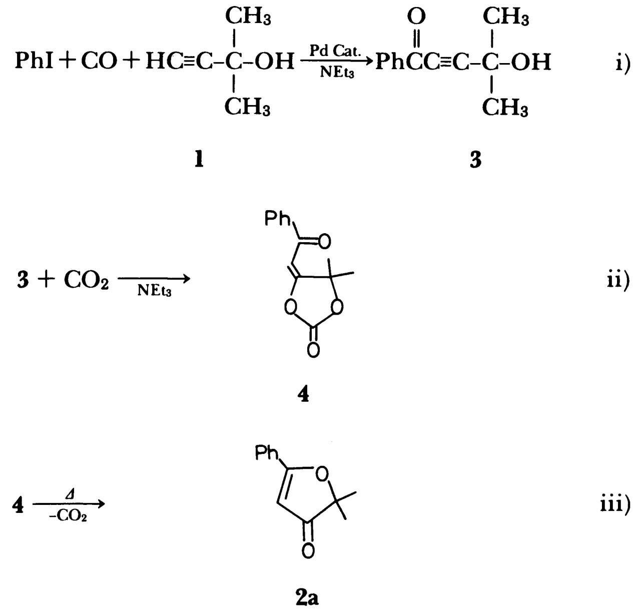


Fig. 2. Reaction of **1** with PhI under CO and CO_2 atmosphere with a $[PdCl_2(PPh_3)_2]$ catalyst.

The relationship between **3** and **4** must be elucidated in the next place. This was made clear by reacting **3** with CO_2 at 70 °C for 1 h in triethylamine in the absence of the catalyst. This procedure gave **4** in 68% isolated yield. The cyclization proceeded even in benzene at the sacrifice of the yield (100 °C, 8 h; 21%).

Thus the following pathway is established for the palladium system.



$$\mathrm{PhI} + \mathrm{CO} + \mathrm{HC{\equiv}C{-}}\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{{-}OH} \xrightarrow[\mathrm{NEt_3}]{\mathrm{Pd\,Cat.}} \mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{C{\equiv}C{-}}\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{{-}OH} \qquad \text{i)}$$

The initial step i) is the formation of the acetylenic ketone **3** from iodobenzene, CO, and 2-methyl-3-butyn-2-ol (**1**). This type of the reaction has been documentated by Tanaka et al.[5] The reaction has been recognized to involve the oxidative addition of a phenyl halide to a low valent metal complex followed by the insertion of CO into the resulting metal–aryl bond to give the aroyl intermediate which is in turn cloven by the attack of an acetylenic molecule to afford the acetylenic ketone. The subsequent step ii) is the triethylamine-assisted intramolecular cycloaddition of the monocarbonate ($PhC(O)C{\equiv}CC(CH_3)_2OC(O)OH$) generated intermediarily from the acetylenic ketone **3** and CO_2 giving the cyclic carbonate **4**.[6] Addition of oxygen-containing nucleophiles to aryl ethynyl ketones has been demonstrated to proceed in a syn fashion.[7] The present cyclization reaction corresponds to the intramolecular version predicting the (*E*)-stereochemistry around the double bond in **4**. The final step iii) was the decarboxylative conversion of **4** into the furanone **2a**. The (*E*)-stereochemistry permits the ready conversion.

There is an apprehension that different pathways might be accomodated in the distinct systems. It seems difficult to elucidate the reaction pathway of every catalytically active system because of the diversity of

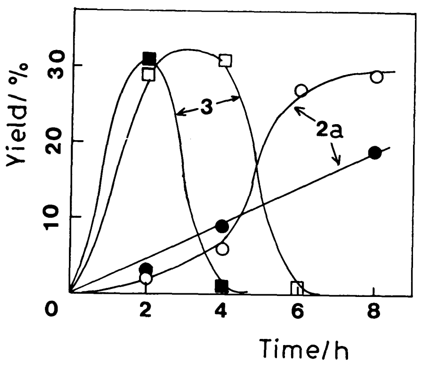


Fig. 3. Reaction of **1** with PhI under CO atmosphere with a $[CoCl_2(PPh_3)_2]$ (□ and ○) or a $[RuCl_2(PPh_3)_3]$ (■ and ●) catalyst.

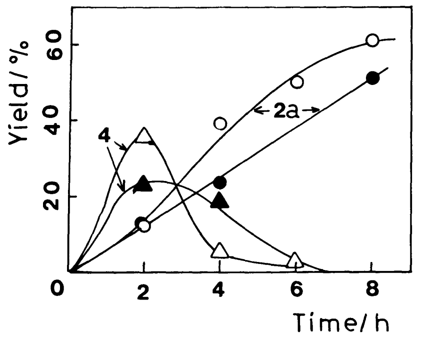


Fig. 4. Reaction of **1** with PhI under CO and CO_2 atmosphere with a $[CoCl_2(PPh_3)_2]$ (△ and ○) or a $[RuCl_2(PPh_3)_3]$ (▲ and ●) catalyst.

metal catalysts. We selected $[RuCl_2(PPh_3)_3]$ and $[CoCl_2(PPh_3)_2]$ as the representative of the Group 8 and 9 metal triad, respectively. The results are shown in Figs. 3 and 4. The same intermediates as the palladium system, **3** and **4**, as well as the similar trends of the reactions were observed. Thus it is evident that the same mechanism is operative at least in these systems, too.

The 3(2*H*)-furanone **2a** occurred even under the atmosphere of CO (Table 1). On careful examination of the products obtained from the reactions performed under CO atmosphere, we found that the cyclic carbonate **4**, albeit in a very small amount, was present in the reaction mixture (by IR; 1855, 1830 cm^{-1}). This indicates the presence of CO_2 in the system. One possible origin is the CO_2 in the air which might be dissolved in triethylamine used as the solvent. To confirm this, the triethylamine distilled under N_2 was subjected to the reaction. However the scope was almost the same under the standard reaction conditions with a $[PdCl_2(PPh_3)_2]$ catalyst. Another one is the water-gas shift reaction, which is known to be catalyzed by transition metal complexes.[8]

$$CO + H_2O \rightleftharpoons CO_2 + H_2$$
$$(\text{or } CO + H_2O + MX_2 \longrightarrow CO_2 + 2HX + M)$$

Table 2. Synthesis of 3(2*H*)-Furanone **2** from Organic Halide (R–X), CO, and **1**[a)]

R	X	Yield of **2**[b)]/%
C_6H_5–	Br	**2a** (35)
C_6H_5–	I	**2a** (48)
p-$CH_3C_6H_4$–	I	**2b** 46
p-ClC_6H_4–	Br	**2c** 68
(*E*)-PhCH=CH–	Br	**2d** 41
1-Naphthyl	Br	**2e** 45
CH_2=$CHCH_2$–	OAc	**2f** 9[c)]

a) **1** 10 mmol, organic halide 10 mmol, CO 10 atm, CO_2 10 atm, $[PdCl_2(PPh_3)_2]$ 0.2 mmol, NEt_3 10 cm^3; 100 °C, 8 h. b) Isolated yield. The figures in the parentheses represent the GLC yield. c) The product was the 1-propenyl derivative.

Consequently eventual water may cause the generation of a trace amount of CO_2. Since the CO_2 produced in this way would work catalytically, a considerable amount of the furanone **2a** could be produced via the steps i), ii), and iii). Thus the reaction under CO atmosphere (10 atm) at 100 °C for 8 h with $[PdCl_2(PPh_3)_2]$ as the catalyst afforded **2a** in 30% yield when care was taken to reduce the eventual water from the chemicals employed by adding appropriate desiccants. With a $[CoCl_2(PPh_3)_2]$ catalyst, the yield of **2a** decreased to 8% with concomitant formation of **3** in 38% yield, supporting the above conjecture.

In order to expand the initial scope of our investigation, several aryl and alkenyl halides were submitted to the reaction. The substrates listed in Table 2 afforded the corresponding furanones in moderate yields with $[PdCl_2(PPh_3)_2]$ as the catalyst. In addition to aryl halides, allyl acetate took part in the reaction yielding the 1-propenyl derivative in a modest yield. *o*-$IC_6H_4NO_2$, *o*-$BrC_6H_4CH_3$, *p*-BrC_6H_4Br, *p*-BrC_6H_4OH, *p*-BrC_6H_4CHO, 2-bromopyridine, and cinnamyl acetate did not afford the corresponding furanones although several of them were consumed. The major difficulty of these compounds in producing the furanone seems to lie in the step i), i.e., acetylenic ketone formation.[5] However further study on the effects of substituents has not been undertaken.

All attempts to utilize 2-propynyl alcohol or 3-butyn-2-ol in place of 2-methyl-3-butyn-2-ol (**1**), for the elaboration of the 3(2*H*)-furanones not disubstituted in the 2-position proved fruitless unfortunately. In conclusion, the present reaction offers a new and facile method for the synthesis of certain simple 3(2*H*)-furanones, e.g., bullatenone. The main feature is the employment of easily available starting materials.

Experimental

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded in chloroform-*d* with JEOL FX-60Q spectrometer with tetramethylsilane as an internal standard. IR and MS spectra were recorded on a JASCO A-3 and JEOL

JMS D-300 spectrometer, respectively. Gas and liquid chromatography was performed on a Hitachi 263-30 gas chromatograph.

Materials. CO and CO_2 gases were used without further purification. Organic halides, 2-propynyl alcohols, and solvents were used as received. In certain cases, $MgSO_4$ (for iodobenzene and **1**) and KOH (for triethylamine) were used as desiccants. Transition metal complexes were synthesized according to the standard methods.

Synthesis of the Furanone 2. The synthesis of 2,2-dimethyl-5-phenyl-3(2*H*)-furanone (**2a**) is typical. Into a 50 cm³ stainless steel autoclave, 2-methyl-3-butyn-2-ol (**1**; 10 mmol), iodobenzene (10 mmol), triethylamine (10 cm³), and $[PdCl_2(PPh_3)_2]$ (0.2 mmol) were charged. Then the air in the autoclave was evacuated by a water aspirator. After CO (10 atm) and CO_2 (10 atm) were introduced, the mixture was agitated at 100 °C for 8 h. GLC analysis (DEGS, 2 m, 190 °C) showed the formation of **2a** in 48% yield. Kugelrohr distillation (150 °C/2 mmHg) followed by recrystallization from hexane gave an analytical sample; (1 mmHg=133.322 Pa). Mp 66.5—67.5 °C (lit,[3] 67.5—68.5 °C). The IR,[9] ^1H NMR,[9] ^{13}C NMR,[10] and mass[11] spectra were consistent with those reported in the literatures. Found: C, 76.33; H, 6.44%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43%.

2,2-Dimethyl-5-(*p*-tolyl)-3(2*H*)-furanone (2b): Prepared from *p*-iodotoluene and isolated by Kugelrohr distillation (125—135 °C/0.2 mmHg). Recrystallization from hexane gave an analytical sample. Mp 65.2—66.4 °C. Found: C, 77.49; H, 7.05%. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. IR ($CDCl_3$) 1690, 1595, 1180 cm⁻¹. ^1H NMR δ=1.47 (s, 6H), 2.40 (s, 3H), 5.87 (s, 1H), 7.20 (d, *J*=8 Hz, 2H), 7.70 (d, *J*=8 Hz, 2H).

5-(*p*-Chlorophenyl)-2,2-dimethyl-3(2*H*)-furanone (2c): Prepared from *p*-bromochlorobenzene and isolated by sublimation under reduced pressure (140—150 °C/1 mmHg). Recrystallization from toluene gave an analytical sample. Mp 218 °C. Found: C, 64.32; H, 5.09; Cl, 16.13%. Calcd for $C_{12}H_{11}ClO_2$: C, 64.73; H, 4.94; Cl, 15.94%. IR (KBr) 1680, 1600, 1325, 1100, 765 cm⁻¹. ^1H NMR δ=1.50 (s, 6H), 5.96 (s, 1H), 7.40 (d, *J*=9.6 Hz, 2H), 7.75 (d, *J*=9.6 Hz, 2H).

(*E*)-2,2-Dimethyl-5-styryl-3(2*H*)-furanone (2d): Prepared from β-bromostyrene and isolated by Kugelrohr distillation (130—150 °C/3 mmHg) followed by column chromatography on silica gel (chloroform). Mp 75.0—76.1 °C. Found: C, 78.92; H, 6.78%. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59%. IR (KBr) 1690, 1630, 1580, 1560, 1380, 1185, 995, 760, 700 cm⁻¹. ^1H NMR δ=1.24 (s, 6H), 5.56 (s, 1H), 6.80 (d, *J*=16.8 Hz, 1H), 7.20—7.70 (m, 6H).

2,2-Dimethyl-5-(1-naphthyl)-3(2*H*)-furanone (2e): Prepared from 1-bromonaphthalene and isolated by column chromatography on silica gel (chloroform). Mp 130.1—131.3 °C. Found: C, 80.75; H, 5.60%. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92%. IR (KBr) 1690, 1570, 1180, 810, 780 cm⁻¹. ^1H NMR δ=1.58 (s, 6H), 5.97 (s, 1H), 7.40—8.40 (m, 7H).

(*E*)-2,2-Dimethyl-5-(1-propenyl)-3(2*H*)-furanone (2f): Prepared from allyl acetate and isolated by column chromatography on silica gel (chloroform). Liquid. Bp 75—85 °C/0.3 mmHg. IR (neat) 1700, 1650, 1390, 1185, 980, 760 cm⁻¹. ^1H NMR δ=1.40 (s, 6H), 1.97 (d, *J*=7 Hz, 3H), 5.40 (s, 1H), 6.23 (d, *J*=16 Hz, 1H), 6.83 (dp, *J*=16 Hz, 7 Hz, 1H).

The Reaction in the Absence of CO_2. The reaction was performed in the absence of CO_2 according to the standard procedure for, for example, 0.5 h with $[PdCl_2(PPh_3)_2]$ as the catalyst. GLC analysis (DEGS, 2 m, 190 °C) showed the formation of 4-hydroxy-4-methyl-1-phenyl-2-pentyn-1-one (**3**) in 66% yield together with the furanone **2a** in 3% yield. The acetylenic ketone **3** was isolated by distillation under reduced pressure. Bp 135—137 °C/2 mmHg. IR (neat) 3400, 2200, 1640, 1270, 1175, 960, 700 cm⁻¹. ^1H NMR δ=1.64 (s, 6H), 2.90 (s, 1H), 7.20—7.60 (m, 3H), 8.00—8.15 (m, 2H).

Short Time Reaction in the Presence of CO and CO_2. When the reaction was discontinued in short time, (*E*)-4-benzoylmethylene-5,5-dimethyl-1,3-dioxolan-2-one (**4**) was obtained together with the furanone **2a** as shown in Fig. 2. The cyclic carbonate **4** was isolated by column chromatography on silica gel eluting with chloroform. This compound was converted completely into the furanone **2a** during the GLC measurement (DEGS, 190 °C). Mp 106—107 °C. IR (KBr) 1855, 1830, 1675, 1620, 1270, 1150, 995 cm⁻¹. ^1H NMR δ=1.87 (s, 6H), 6.80 (s, 1H), 7.20—8.00 (m, 5H). ^{13}C NMR δ=24.0, 88.8, 99.6, 128.0, 128.7, 133.3, 138.0, 149.8, 167.1, 188.1. The reactions in the presence or absence of CO_2 with the other catalysts, for example $[CoCl_2(PPh_3)_2]$ and $[RuCl_2(PPh_3)_3]$, were performed in the similar manner as above.

Synthesis of the Cyclic Carbonate 4 from the Acetylenic Ketone 3 and CO_2. **3** (5 mmol) and triethylamine (5 cm³) were placed in an autoclave. After the introduction of CO_2 (10 atm), the autoclave was heated at 70 °C for 1 h. Column chromatography of the reaction mixture on silica gel (hexane/ethyl acetate=5) gave the cyclic carbonate **4** in 68% yield. On the other hand the reaction of **3** (5 mmol) with CO_2 (10 atm) in benzene (5 cm³) at 100 °C for 8 h gave **4** in 21% yield.

Decarboxylative Conversion of the Cyclic Carbonate 4 into the Furanone 2a. Into an autoclave, **4** (105 mg, 0.45 mmol), $[Pd(PPh_3)_4]$ (2 molar%), and trietylamine (5 cm³) were placed. After CO (10 atm) was introduced, the autoclave was heated at 100 °C for 1 h. This procedure gave the furanone **2a** in 73% yield. The degradation of **4** under CO_2 atmosphere (10 atm) led to the formation of **2a** in 75% yield under the similar conditions. The degradation at 150 °C was performed as follows. Into a 50 cm³ round bottomed flask connected with a gas buret, **4** (218 mg, 0.938 mmol) was placed and heated at about 150 °C for 20 min in an oil bath. The CO_2 gas evolved was 122.1 cm³ at 22 °C (0.91 mmol, 97%) and the residue weighed was 172 mg (0.936 mmol, 100%). IR analysis confirmed the complete conversion of **4** into the furanone **2a**.

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