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Rhodium-catalyzed synthesis of 2(5*H*)-furanones from terminal alkynes and non-substituted alkynes under water-gas shift reaction conditions

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Abstract

Rhodium-catalyzed synthesis of 2(5*H*)-furanones from alkynes under water-gas shift reaction conditions was studied. By improving the reaction conditions for internal alkynes reported previously, the reaction could be extended to terminal alkynes. Terminal alkynes are selectively converted into 3- and 4-substituted 2(5*H*)-furanones (**2** and **3**). When acetylene itself is used, 2(5*H*)-furanone (**2n**) is obtained in a good yield. Examination of reaction solutions by IR spectroscopy and some other experimental findings suggest that the active species would be an alkyne-coordinated monomeric rhodium anion. A new reaction path is proposed.

Key words: Catalysis; Furanone; Oxygenate compounds; Rhodium complexes; Alkyne complexes

Introduction

Carbonylation of alkynes with carbon monoxide in the presence of a soluble transition metal catalyst is an important synthetic route to a variety of oxygenates such as aldehydes, ketones, carboxylates and lactones [1]. We have reported the catalytic preparation of 3,4-disubstituted 2(5*H*)-furanones by the rhodium-catalyzed reductive carbonylation of internal alkynes under water-gas shift reaction conditions, but attempts to obtain furanones from terminal alkynes such as phenylacetylene were not successful under the reported reaction conditions [2].

2(5*H*)-Furanones are one of the most important synthetic targets because they are useful synthetic intermediates and an important class of naturally occurring compounds, some derivatives of which possess significant biological activities [3]. Thus, we have performed the re-investigation of reaction conditions and found that the reaction can be extended as a new general method for the selective synthesis of 2(5*H*)-furanones from terminal and non-substituted alkynes in addition to internal alkynes. The preliminary results have already been reported [4].

We report herein the details of the synthesis of 2(5*H*)-furanones from terminal and non-substituted alkynes by rhodium-catalyzed carbonylation under water-gas shift reaction conditions. A new reaction mechanism of the carbonylation is also discussed based on the results of some mechanistic examinations.

Experimental

Melting points were recorded on a Yanagimoto micro melting point apparatus and are not corrected. ^{1}H NMR spectra were recorded with a Bruker AM-360 instrument using tetramethylsilane as an internal standard in $CDCl_3$. IR spectra were taken on a Hitachi 295 infrared spectrophotometer. GC-MS spectra were recorded with a Shimazu GC MS-2000 apparatus. GC analyses were carried out on a Shimazu GC-12A, using a helium carrier gas flow. The column used was a 5-m 20% Silicon SE-30. Elemental analyses were performed by the Material Analysis Center, ISIR, Osaka University.

Materials

$[Rh(CO)_2Cl]_2$ [5], $Rh_4(CO)_{12}$ [6] and $Rh_6(CO)_{16}$ [7] were prepared according to the reported procedures. Substituted phenylacetylenes were prepared by the procedure developed in our laboratory [8]. All other chemicals were commercially available reagents of the highest purity and were used without purification.

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General procedure for preparation of 2(5H)-furanones from terminal alkyne

Into a 100 ml stainless steel autoclave were added 15 mmol of alkyne (**1**), 10 mg (9.4×10^{-3} mmol) of $Rh_6(CO)_{16}$, 0.3 ml (2.2 mmol) of Et_3N, 45 ml of dioxane and 1.5 ml (83 mmol) of H_2O. The autoclave was flushed three times with CO and then charged at room temperature to an initial CO pressure of 100 atm. The reaction was carried out at 80 °C for 5 h. GC analysis of the resulting solution was carried out and the results are shown in Table 1. After removal of the solvent, 3- and 4-substituted 2(5*H*)-furanones (**2** and **3**) were obtained by column chromatography on silica gel. They were purified by recrystallization or distillation under reduced pressure. ^1H NMR spectra of the furanones are collected in Table 2.

Synthesis of 3-phenyl-2(5H)-furanone (2b) and 4-phenyl-2(5H)-furanone (3b)

The general procedure was followed using 1.53 g (15 mmol) of phenylacetylene (**1b**). After separation by column chromatography, **2b** and **3b** were obtained in yields of 0.95 g (39.5%) and 0.65 g (27%), respectively.

2b: colorless needles from ethanol, m.p. 84–86 °C (lit. 81–84 °C [9]); IR (Nujol) $\nu(C{=}O)$ 1760 cm^{-1}; MS *m*/*z* 160 (M^+).

3b: colorless leaves from ethanol, m.p. 93.5–94.5 °C (lit. 95–97 °C [9]); IR (Nujol) $\nu(C{=}O)$ 1750 cm^{-1}; MS *m*/*z* 160 (M^+).

Synthesis of 3-(p-tolyl)-2(5H)-furanone (2c) and 4-(p-tolyl)-2(5H)-furanone (3c)

The general procedure was followed using 1.75 g (15 mmol) of *p*-tolylacetylene (**1c**). After separation by column chromatography, **2c** and **3c** were obtained in yields of 1.136g (43%) and 0.93 g (35%), respectively.

2c: colorless needles from ethanol, m.p. 109.4–110.4 °C; IR (Nujol) $\nu(C{=}O)$ 1760 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 76.15; H, 5.94%.

3c: colorless needles from ethanol, m.p. 115.2–115.7 °C (lit. 114–116 °C [10]); IR (Nujol) $\nu(C{=}O)$ 1740 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 76.05; H, 5.96%.

Synthesis of 3(m-tolyl)-2(5H)-furanone (2d) and 4-(m-tolyl)-2(5H)-furanone (3d)

The general procedure was followed using 1.75 g (15 mmol) of *m*-tolylacetylene (**1d**). After separation by column chromatography, **2d** and **3d** were obtained in yields of 0.996 g (38%) and 0.957 g (36%), respectively.

2d: colorless crystals from ethanol, m.p. 83.5–84.0 °C; IR (Nujol) $\nu(C{=}O)$ 1755 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 76.02; H, 5.99%.

3d: colorless crystals from ethanol, m.p. 86.0–86.2 °C (lit. 87–88 °C [10]); IR (Nujol) $\nu(C{=}O)$ 1755 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 76.11; H, 5.96%.

Synthesis of 3-(o-tolyl)-2(5H)-furanone (2e) and 4-(o-tolyl)-2(5H)-furanone (3e)

The general procedure was followed using 1.75 g (15 mmol) of *o*-tolylacetylene (**1e**). After separation by column chromatography, **2e** and **3e** were obtained in yields of 0.795 g (30%) and 1.329 g (51%), respectively.

2e: colorless liquid: IR (liquid film) $\nu(C{=}O)$ 1760 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 74.39; H, 5.37%.

3e: colorless crystals from ethanol, m.p. 68.0–69.0 °C; IR (Nujol) $\nu(C{=}O)$ 1740 cm^{-1}; MS *m*/*z* 174 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 76.06; H, 5.99%.

Synthesis of 3-(p-methoxyphenyl)-2(5H)-furanone (2f) and 4-(p-methoxyphenyl)-2(5H)-furanone (3f)

The general procedure was followed using 1.98 g (15 mmol) of *p*-methoxyphenylacetylene (**1f**). After separation by column chromatography, **2f** and **3f** were obtained in yields of 0.90 g (32%) and 0.635 g (22%), respectively.

2f: pale yellow needles from ethanol, m.p. 121.6–122.2 °C; MS *m*/*z* 190 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.42; H, 5.26%.

3f: pale red needles from ethanol, m.p. 119.1–119.8 °C (lit. 119.5–120 °C) [11]; MS *m*/*z* 190 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.41; H, 5.29%.

Synthesis of 3-(o-methoxyphenyl)-2(5H)-furanone (2g) and 4-(o-methoxyphenyl)-2(5H)-furanone (3g)

The general procedure was followed using 1.98 g (15 mmol) of *o*-methoxyphenylacetylene (**1g**). After separation by column chromatography, **2g** and **3g** were obtained in yields of 0.993 g (34%) and 1.016 g (35%), respectively.

2g: colorless plates from ethanol, m.p. 86.1–86.6 °C; IR (Nujol) $\nu(C{=}O)$ 1750 cm^{-1}; MS *m*/*z* 190 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.49; H, 5.28%.

3g: colorless plates from ethanol, m.p. 94.7–95.2 °C; IR (Nujol) $\nu(C{=}O)$ 1745 cm^{-1}; MS *m*/*z* 190 (M^+). *Anal.* Calc. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.45; H, 5.32%.

Synthesis of 3-(p-chlorophenyl)-2(5H)-furanone (2h) and 4-(p-chlorophenyl)-2(5H)-furanone (3h)

The general procedure was followed using 2.06 g (15 mmol) of *p*-chlorophenylacetylene (**1h**). After separation by column chromatography, **2h** and **3h** were obtained in yields of 0.829 g (28%) and 1.048 g (36%), respectively.

2h: colorless needles from ethanol, m.p. 94.2–94.7 °C; IR (Nujol) ν(C=O) 1755 cm^{-1}; MS *m/z* 196, 194 (M^+). *Anal.* Calc. for $C_{10}H_7ClO_2$: C, 61.72; H, 3.63; Cl, 18.22. Found: C, 61.63; H, 3.54; Cl, 18.02%.

3h: colorless needles from ethanol, m.p. 173.3–174.3 °C; IR (Nujol) ν(C=O) 1750 cm^{-1}; MS *m/z* 196, 194 (M^+). *Anal.* Calc. for $C_{10}H_7ClO_2$: C, 61.72; H, 3.63; Cl, 18.22. Found: C, 61.45; H, 3.34, Cl, 18.45%.

Synthesis of 3-(n-butyl)-2(5H)-furanone (2i) and 4-(n-butyl)-2(5H)-furanone (3i)

The general procedure was followed using 1.26 g (15 mmol) of 1-hexyne (**1i**). After separation by column chromatography, **2i** and **3i** were obtained in yields of 0.572 g (27%) and 0.923 g (44%), respectively.

2i: colorless liquid; IR (liquid film) ν(C=O) 1755 cm^{-1}; MS *m/z* 140 (M^+).

3i: colorless liquid; IR (liquid film) ν(C=O) 1760 cm^{-1}; MS *m/z* 140 (M^+).

Synthesis of 3-(n-hexyl)-2(5H)-furanone (2j) and 4-(n-hexyl)-2(5H)-furanone (3j)

The general procedure using 1.71 g (15 mmol) of 1-octyne (**1j**). After separation by column chromatography, **2j** and **3j** were obtained in yields of 0.841 g (32%) and 1.486 g (57%), respectively.

2j: colorless liquid; IR (liquid film) ν(C=O) 1760 cm^{-1}; MS *m/z* 168 (M^+). *Anal.* Calc. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.13; H, 9.50%.

3j: colorless liquid; IR (liquid film) ν(C=O) 1760 cm^{-1}; MS *m/z* 168 (M^+). *Anal.* Calc. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.25: H, 9.48%.

Synthesis of 3-(t-butyl)-2(5H)-furanone (2k) and 4-(t-butyl)-2(5H)-furanone (3k)

The general procedure was followed using 1.31 g (15 mmol) of 3,3-dimethyl-1-butyne (**1k**). After separation by column chromatography, **2k** and **3k** were obtained in yields of 1.511 g (68%) and 0.65 g (29%), respectively.

2k: colorless liquid; IR (liquid film) ν(C=O) 1755 cm^{-1}.

3k: colorless liquid; IR (liquid film) ν(C=O) 1760 cm^{-1}.

Synthesis of 3-(1-methyl-1-hydroxyethyl)-2(5H)-furanone (2l) and 4-(1-methyl-1-hydroxyethyl)-2(5H)-furanone (3l)

The general procedure was followed using 1.27 g (15 mmol) of 2-methyl-3-butyn-2-ol (**1l**). **2l** and **3l** were obtained by GC in yields of 57% and 31%, respectively. After column chromatography on silica gel, 1.43 g (67%) of a mixture of **2l** and **3l** was obtained. By repeated column chromatography and vacuum distillation, **2l** and **3l** could be purified in low yields.

2l: colorless liquid; IR (liquid film) ν(OH) 3700–3150, ν(C=O) 1755 cm^{-1}.

3l: colorless liquid; IR (liquid film) ν(OH) 3700–3150, ν(C=O) 1750 cm^{-1}.

Synthesis of 3-hydroxymethyl-2(5H)-furanone (2m) and 4-hydroxymethyl-2(5H)-furanone (3m)

The general procedure was followed using 0.85 g (15 mmol) of propargylalcohol (**1m**). **2m** and **3m** were obtained by GC in yields of 27% and 33%, respectively. After column chromatography on silica gel, 0.56 g (33%) of a mixture of **2m** and **3m** was obtained. Attempts to separate **2m** from **3m** gave pure **2m** and a mixture of **2m** and **3m** (1:4).

2m: colorless liquid; IR (liquid film) ν(OH) 3700–3000, ν(C=O) 1740 cm^{-1}.

3m: colorless liquid; IR (liquid film) ν(OH) 3700–3000, ν(C=O) 1750 cm^{-1}.

Synthesis of 2(5H)-furanone (2n)

Into a 100 ml stainless steel autoclave were placed $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), dioxane (45 ml), Et_3N (2.2 mmol), and H_2O (83 mmol). After the reaction system was flushed several times with acetylene gas, acetylene (5 atm, *c.* 13 mmol) was introduced. Then CO was charged to an initial pressure of 100 atm. The reaction was carried out at 80 °C for 5 h. GC analysis of the resultant reaction mixture showed the formation of 0.983 g (90% yield) of **2n**. After evaporation of the solvent under an ordinary pressure, distillation under a reduced pressure (70 °C/10 mm Hg) gave 0.603 g (55% yield) of **2n**. The product was identified by comparison with the spectra of a commercially available sample. When the higher concentration of acetylene was introduced, polymeric materials were formed and the yield of **2n** was decreased.

Synthesis of 3,4-diphenyl-2(5H)-furanone (2a)

The general procedure was followed using $Rh_6(CO)_{16}$ (10.6 mg, 1.0×10^{-2} mmol), diphenylacetylene (**1a**) (2.68 g, 15 mmol), Et_3N (0.3 ml, 2.2 mmol), H_2O (1.5 ml, 8.3 mmol) and dioxane (45 ml). After separation by column chromatography, **2a** was obtained in an isolated yield of 1.12 g (32%) and 1.73 g (64%) of **1a** was recovered.

Reactions of 1b in various reaction conditions

Using the general procedure described above as the standard reaction conditions, reactions of **1b** were carried out in various conditions and the resultant reaction solutions were analyzed by GC. The results are shown in Tables 3–10.

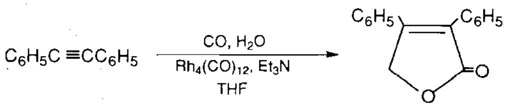
IR spectra measurement of the reaction solution

(i) IR spectra of solution obtained by catalytic carbonylation. The following reagents and solvent were introduced into a 20 ml glass ampoule: crystals of $Rh_6(CO)_{16}$ (5×10^{-3} mmol), THF or chloroform (5 ml), 3-hexyne or **1b** (1.7 mmol), Et_3N (2.4×10^{-1} mmol) and H_2O (10 mmol). The ampoule was placed in a 100 ml stainless steel autoclave. The reaction was carried out under CO (100 atm) at 50 °C for 2 h. IR spectra of the resultant reaction mixture were recorded.

(ii) IR spectra of solution in the reaction at ordinary temperature and pressure. A THF solution (5 ml) of 3-hexyne (1.7 mmol), Et_3N (2.4×10^{-1} mmol), and H_2O (10 mmol) was treated with $Rh_6(CO)_{16}$ (5×10^{-3} mmol) under an atmospheric pressure of CO at room temperature. IR spectra of the solution were taken at appropriate intervals.

Results and discussion

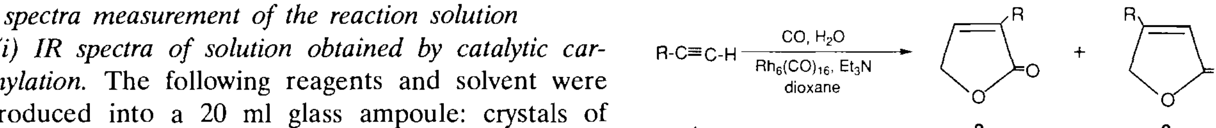
When a mixture of diphenylacetylene (**1a**) and a catalytic amount of $Rh_4(CO)_{12}$ in the presence of Et_3N in THF was heated at 100 °C under a pressure of CO (100 atm), 3,4-diphenyl-2(5*H*)-furanone (**2a**) was obtained in a good yield [2]. A variety of internal alkynes were successfully employed in place of diphenylacetylene, although attempts to obtain furanones from terminal and non-substituted alkynes were not successful under the same conditions.



(1)

1a **2a**

After re-investigations of reaction conditions using phenylacetylene (**1b**), we have found new conditions under which **1b** gives a mixture of 3- and 4-phenyl-2(5*H*)-furanones (**2b** and **3b**) in good yields. In a typical procedure, **1b** (15 mmol) was treated with water (83 mmol) and CO (100 atm) in dioxane (45 ml) containing Et_3N (2.2 mmol) at 80 °C for 5 h in the presence of $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol). The reaction proceeded smoothly and gave **2b** and **3b** in yields of 50% and 43%, respectively. Other terminal alkynes and non-substituted alkyne gave the corresponding furanones **2** and **3** in good yields under the same reaction conditions. The results obtained are summarized in Table 1. A variety of phenylacetylene derivatives (**1b**–**1h**) gave furanones in good yields.



(2)

1 **2** **3**

1b: R=C_6H_5; **1c**: R=*p*-MeC_6H_4; **1d**: R=*m*-MeC_6H_4; **1e**: R=*o*-MeC_6H_4; **1f**: R=*p*-$MeOC_6H_4$; **1g**: R=*o*-$MeOC_6H_4$; **1h**: R=*p*-ClC_6H_4; **1i**: R=*n*-C_4H_9 **1j**: R=*n*-C_6H_{13}; **1k**: R=*t*-C_4H_9; **1*l***: R=$HOCMe_2$; **1m**: R=$HOCH_2$; **1n**: R=H

1-Alkynes such as **1i**, **1j** and **1k** also gave the corresponding furanones in good yields. It is of interest that alkynols (**1l** and **1m**) gave the furanones in which an alcoholic group was intact for the construction of a furanone ring. It has been reported that the Pd-catalyzed cyclo-carbonylation of alkynols gave unsaturated lactones in which the oxygen atom of an alcoholic group was incorporated into the lactone ring [12, 13].

It is noticeable that non-substituted alkyne (**1n**), which is highly reactive and often produces a polymeric material in other systems, also afforded furanone (**2n**) in a good yield under these reaction conditions.

The ratios of two regioisomers (**2** and **3**) produced in the reactions were about 1/1 for phenylacetylene derivatives and seem not to be affected by the electronic and steric nature of the substituents on the phenyl ring of aromatic acetylenes. In the case of alkyl substituted acetylenes, the ratios of **2**/**3** were about 3/7 for straight-chain alkyl substituted acetylenes, while 7/3 for a t-butyl substituted acetylene.

The structures of **2** and **3** were deduced from the IR, ^1H NMR and mass spectra. Their IR spectra reveal a characteristic C=O stretching band of unsaturated lactones at 1750–1760 cm^{-1}. ^1H NMR spectra of **2** and **3** are shown in Table 2. In the ^1H NMR spectra of a

TABLE 1. Synthesis of 2(5*H*)-furanones from alkynes[a]

Entry	Alkyne	Conversion (%)	Furanone	Selectivity[b] (%)	2:3[d]
1	**1a**	36	**2a**	89[c]	
2	**1b**	100	**2b**+**3b**	93	54:46
3	**1c**	100	**2c**+**3c**	87	54:46
4	**1d**	100	**2d**+**3d**	98	47:53
5	**1e**	100	**2e**+**3e**	91	37:63
6	**1f**	100	**2f**+**3f**	75	49:51
7	**1g**	93	**2g**+**3g**	77	42:58
8	**1h**	100	**2h**+**3h**	85	49:51
9	**1i**	100	**2i**+**3i**	92	30:70
10	**1j**	100	**2j**+**3j**	99	34:66
11	**1k**	100	**2k**+**3k**	99	73:27
12	**1l**	100	**2l**+**3l**	88	61:39
13	**1m**	100	**2m**+**3m**	60	45:55
14	**1n**		**2n**	90	

[a] Alkyne (15 mmol), $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), H_2O (83 mmol), Et_3N (2.2 mmol), dioxane (45 ml), CO (100 atm), 80 °C, 5 h. [b] Determined by GC analysis, based on alkyne consumed. [c] Calculated from isolated yield. [d] Molar ratio of the regioisomers.

TABLE 2. ^{1}H NMR spectra of 3- and 4-substituted 2(5*H*)-furanones (**2** and **3**)

Compound	^{1}H NMR (δ)			
	H^3	H^4	H^5	R
2b		7.64 (t)	4.93 (d, 2H)	7.37–7.45 (m, 3H); 7.83–7.87 (m, 2H)
2c		7.58 (t)	4.90 (d, 2H)	2.38 (s, 3H); 7.21–7.25 (m, 2H); 7.74–7.76 (m, 2H)
2d		7.61 (t)	4.90 (d, 2H)	2.38 (s, 3H); 7.19–7.32 (m, 2H); 7.60–7.66 (m, 2H)
2e		7.43 (t)	4.94 (d, 2H)	2.32 (s, 3H); 7.19–7.35 (m, 4H)
2f		7.51 (t)	4.90 (d, 2H)	3.84 (s, 3H); 6.92–6.96 (m, 2H); 7.81–7.85 (m, 2H)
2g		7.98 (t)	4.93 (d, 2H)	3.89 (s, 3H); 6.96–7.06 (m, 2H); 8.14–8.16 (m, 2H)
2h		7.66 (t)	4.94 (d, 2H)	7.37–7.41 (m, 2H); 7.80–7.83 (m, 2H)
2i		7.10 (t)	4.76–4.78 (m, 2H)	0.93 (t, 3H); 1.38–2.33 (m, 6H)
2j		7.12 (t)	4.76 (m, 2H)	0.87–0.91 (m, 3H); 1.30–2.29 (m, 10H)
2k		7.08 (t)	4.71 (d, 2H)	1.26 (s, 9H)
2l		7.24 (t)	4.80 (d, 2H)	1.52 (s, 6H); 2.90–3.26 (br, 1H)
2m		7.47 (m)	4.88 (m)	3.35 (s, 1H); 4.42 (m, 2H)
3b	6.38 (t)		5.23 (d, 2H)	7.45–7.54 (m, 5H)
3c	6.32 (t)		5.20 (d, 2H)	2.41 (s, 3H); 7.26–7.41 (m, 4H)
3d	6.36 (t)		5.22 (d, 2H)	2.41 (s, 3H); 7.31–7.39 (m, 4H)
3e	6.27 (t)		5.19 (d, 2H)	2.48 (s, 3H); 7.26–7.38 (m, 4H)
3f	6.22 (t)		5.18 (d, 2H)	3.87 (s, 3H); 6.95–7.48 (m, 4H)
3g	6.56 (t)		5.27 (d, 2H)	3.93 (s, 3H); 7.00–7.49 (m, 4H)
3h	6.38 (t)		5.21 (d, 2H)	7.46 (m, 4H)
3i	5.38–5.84 (m)		4.74 (m, 2H)	0.95 (t, 3H); 1.40–2.42 (m, 6H)
3j	5.83–5.84 (m)		4.75 (d, 2H)	0.90 (t, 3H); 1.29–2.42 (m, 10H)
3k	5.80 (m)		4.84 (d, 2H)	1.24 (s, 9H)
3l	5.90 (m)		4.93 (d, 2H)	1.52 (s, 6H); 2.3–2.8 (s, 1H)
3m	6.01–6.03 (m)		4.89 (m, 2H)	3.60 (s, 1H); 4.58–4.60 (m, 2H)

series of **2**, the signals due to an olefinic proton appear at δ 7.0–8.0, while in those of a series of **3**, the signals appear at δ 5.8–6.6. The signals due to methylene protons of both series of furanones appear at δ 4.7–5.3. The olefinic proton signals of 2(5*H*)-furanone itself (**2n**) are observed at δ 7.63 and 6.15 ppm, which are assignable to those of the H^4 and H^3 protons, respectively. The methylene proton signal is observed at δ 4.92 ppm, which is assignable to that of the H^5 proton [14]. The products **2** and **3** were therefore deduced to be 3- and 4-substituted 2(5*H*)-furanones, respectively.

Internal alkyne (**1a**) showed a lower reactivity than terminal alkynes. But in terms of efficiency of the catalyst, the new reaction conditions show an increase of turnover number per Rh atom by 300% over the previous reaction conditions [2].

Consequently, not only internal alkynes but also terminal and non-substituted ones can be selectively converted to 2(5*H*)-furanones by catalysis with rhodium carbonyl complexes under water-gas shift reaction conditions and the present reaction may offer a useful synthetic method for 2(5*H*)-furanones.

In the course of the determination of optimum conditions, we observed that a variety of factors affected the reaction. These are discussed in the following sections.

Effect of reaction temperature

Table 3 contains the results of a series of experiments carried out to examine the influence of reaction temperature on the carbonylation of **1b**. A temperature of about 60–80 °C is optimal for the furanone formation. The conversion was decreased but the selectivity did not change at temperatures lower than 60 °C and both

TABLE 3. Effect of temperature on the catalytic carbonylation of phenylacetylene[a]

Entry	Temperature (°C)	Conversion (%)	Selectivity[b] (%)	**2b**:**3b**
1	40	49	80	62:38
2	50	83	83	62:38
3	60	97	93	57:43
4	70	100	80	57:43
5	80	100	92	50:50
6	90	100	82	49:51
7	100	100	72	41:59
8	110	100	59	46:54
9	120	74	35	42:58
10	160	32	15	46:54

[a] Phenylacetylene (15 mmol), $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), H_2O (83 mmol), Et_3N (2.2 mmol), dioxane (45 ml), CO (100 atm), 5 h. [b] Determined by GC analysis, based on phenylacetylene consumed.

the conversion and the selectivity were decreased at temperatures higher than 100 °C.

Effect of solvents

The reaction activity and the reaction selectivity are markedly influenced by the nature of the solvents as shown in Table 4. Solvents having a smaller dielectric constant gave good results. In spite of their immiscibility with water, benzene and chloroform showed excellent results, but the reaction did not take place in hexane perhaps due to insolubility of the catalyst. The trends of higher regioselectivity in favor of **2** but lower activity and selectivity were observed for more polar solvents.

Effect of the concentration of Et_3N

Table 5 shows the effect of the amount of Et_3N. The reaction did not proceed without Et_3N. Addition of Et_3N showed a remarkable effect. The optimal concentration of amine may be 0.05 M (entry 5), which corresponds to about 4% of the amine concentration in the previously reported reactions for internal alkynes [2]. The presence of a large amount of amine caused a decrease in the activity and the selectivity.

TABLE 4. Effect of various solvents on the carbonylation of phenylacetylene[a]

Entry	Solvent	Dielectric constant[b]	Conversion (%)	Selectivity[c] (%)	**2b**:**3b**
1	Chloroform	4.8	100	81	35:65
2	Benzene	2.3	100	78	44:56
3	Dioxane	2.2	83	83	62:38
4	Diethylether	4.3	76	70	65:35
5	THF	7.6	32	48	84:16
6	Acetone	20.7	20	28	87:13
7	2-Ethoxyethanol	29.6	20	24	93:7
8	DMF	36.7	0	0	
9	2-Methyl-2-butanol	5.8	57	69	80:20
10	t-Butanol	12.5	45	70	85:15
11	n-Propanol	20.3	38	52	81:19
12	Ethanol	24.6	26	46	79:21
13	Methanol	32.7	21	40	72:28

[a]Phenylacetylene (15 mmol), $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), H_2O (83 mmol), Et_3N (2.2 mmol), solvent (45 ml), CO (100 atm), 50 °C, 5 h. [b]The values are quoted from the literature [15]. [c]Determined by GC analysis, based on phenylacetylene consumed.

TABLE 5. Effect of triethylamine on the catalytic carbonylation of phenylacetylene[a]

Entry	Et_3N (mmol)	Conversion (%)	Selectivity[b] (%)	**2**:**3**
1	0	4	0	
2	0.2	39	50	55:45
3	0.4	56	74	48:52
4	0.7	71	80	55:45
5	2.2	83	83	62:38
6	13.0	56	76	62:38
7	38.0	41	60	62:38

[a]Phenylacetylene (15 mmol), $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), H_2O (83 mmol), Et_3N+dioxane (45 ml), CO (100 atm), 50 °C, 5 h. [b]Determined by GC analysis, based on phenylacetylene consumed.

Effect of the concentration of alkyne

Table 6 contains the results of the reactions with varying concentration of **1b**. A higher concentration of **1b** decreased the selectivity, although the activity was not influenced so much.

Effect of the amount of water

One molecule of water is required to give furanone from one molecule of alkyne in this reaction. The results shown in Table 7 indicate that the presence of water equivalent to alkyne is sufficient to complete the reaction. When a larger amount of water is present, both the reaction activity and the reaction selectivity were decreased although the regioselectivity was increased in favor of **2b**.

Effect of the concentration of catalyst

The effect of the catalyst concentration is shown in Table 8. The results show that the lower concentration of catalyst is favorable to obtain the higher turnover

TABLE 6. Effect of the concentration of phenylacetylene on the catalytic carbonylation of phenylacetylene[a]

Entry	Phenylacetylene (mmol)	Phenylacetylene (M)	Conversion (%)	Selectivity[b] (%)	Turnover number[c]	**2b**:**3b**
1	10	0.21	76	80	130	60:40
2	15	0.31	83	83	220	62:38
3	30	0.63	50	78	260	56:44
4	45	0.94	43	60	250	55:45
5	90	1.88	23	54	230	55:45

[a]$Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), H_2O (83 mmol), Et_3N (2.2 mmol), dioxane (45 ml), CO (100 atm), 50 °C, 5 h. [b]Based on phenylacetylene consumed. [c]Mol/mol of $Rh_6(CO)_{16}$/h.

TABLE 7. Effect of water on the catalytic carbonylation of phenylacetylene[a]

Entry	H_2O (equiv. to alkyne)	Conversion (%)	Selectivity[b] (%)	**2b**:**3b**
1	0	15	21	42:58
2	0.5	51	84	40:60
3	1.0	72	84	43:57
4	2.0	83	87	48:52
5	5.6	83	83	62:38
6	11.0	59	76	69:31
7	17.0	48	69	78:22

[a]Phenylacetylene (15 mmol), $Rh_6(CO)_{16}$ (9.4×10^{-3} mmol), Et_3N (2.2 mmol), dioxane (45 ml), CO (100 atm), 50 °C, 5 h. [b]Based on phenylacetylene consumed.

TABLE 8. Effect of catalyst concentration on the carbonylation of phenylacetylene[a]

Entry	$Rh_6(CO)_{16}$ (M)	Conversion (%)	Selectivity (%)	Turnover number[b]	**2b**:**3b**
1	0.2×10^{-4}	18	64	350	59:41
2	0.7×10^{-4}	42	84	350	54:46
3	1.1×10^{-4}	53	84	280	53:47
4	2.1×10^{-4}	83	83	220	62:38
5	4.2×10^{-4}	84	84	110	58:42
6	9.6×10^{-4}	96	80	54	61:39

[a]Phenylacetylene (15 mmol), H_2O (83 mmol), Et_3N (2.2 mmol), dioxane (45 ml), CO (100 atm), 50 °C, 5 h. [b]Mol/mol of $Rh_6(CO)_{16}$/h.

TABLE 9. Initial rates for the formation of furanones by different rhodium catalysts[a]

Solvent	Catalyst	Conversion (%)	Selectivity[b] (%)	**2b**:**3b**
THF	$Rh_6(CO)_{16}$	4	100	69:31
	$Rh_4(CO)_{12}$	7	99	85:15
	$[Rh(CO)_2Cl]_2$	10	98	80:20
Dioxane	$Rh_6(CO)_{16}$	8	99	60:40
	$Rh_4(CO)_{12}$	21	98	57:43
	$[Rh(CO)_2Cl]_2$	31	94	51:43
$CHCl_3$	$Rh_6(CO)_{16}$	12	100	25:75
	$Rh_4(CO)_{12}$	41	86	31:69
	$[Rh(CO)_2Cl]_2$	46	83	24:76

[a]Phenylacetylene (5 mmol), solvent (15 ml), Et_3N (0.7 mmol), H_2O (27.7 mmol), catalyst (1.88 mg-atom Rh), CO (100 atm), 50 °C, 1 h. [b]Based on phenylacetylene consumed.

value. Although the catalyst concentration of about 8×10^{-3} g-atm Rh/l was used in our previous work [2], sufficient activity was obtained in the presence of catalyst of about 1.3×10^{-3} g-atm Rh/l (entry 4) in the improved reaction conditions.

Initial rates for the formation of furanones by different catalyst precursors

Other rhodium carbonyl complexes, such as $Rh_4(CO)_{12}$ and $[Rh(CO)_2Cl]_2$, could be used as the catalyst. When the reactions were carried out at 80 °C for 5 h, the activity and the selectivity of these complexes did not vary greatly from those of $Rh_6(CO)_{16}$, because under the present conditions the reaction producing an active species from a catalyst precursor probably attained equilibrium very rapidly. However, when the reactions were carried out at 50 °C for 1 h, the initial rates were found to be different with the catalyst precursors. As shown in Table 9, the initial rates were increased in the order of $Rh_6(CO)_{16} \ll Rh_4(CO)_{12} < [Rh(CO)_2Cl]_2$ in every solvent used. These results indicate that the optimum conditions for the reaction are realized when the reaction is carried out using $[Rh(CO)_2Cl]_2$ in chloroform, although the reactions described above were carried out using $Rh_6(CO)_{16}$ in dioxane which is miscible with water to afford a homogeneous reaction system.

In addition to the experiments which led to the optimization of reaction conditions for the catalytic formation of furanones from terminal alkynes, some experiments were carried out for the purpose of obtaining information about the mechanism of this reaction. The results of the experiments are described in the following sections.

Effect of the addition of alkyl ammonium chloride

As shown in Table 10, the addition of $[Et_4N]^+Cl^-$ to the reaction system caused a decrease of both the reaction activity and the selectivity (entry 2). On the contrary, addition of an even larger amount of $[Et_3NH]^+Cl^-$ had no effect on the activity and the selectivity for furanone formation (entry 3), suggesting that the active species may be an anion and hydrogen must be involved in its counter cation. A similar observation has been reported; that is, in aqueous solutions $[Et_3NH]^+[HFe(CO)_4]^-$ rapidly reduces 1-pentanal to 1-butanol while the corresponding sodium salt $NaHFe(CO)_4$ was unreactive under the same conditions [16, 17].

IR spectra of the reaction solution

In order to obtain information about the catalyst species, we examined the IR spectra of the solution in the midst of the catalytic reaction. As dioxane has strong absorption bands in the range 2000–1800 cm^{-1}, THF or chloroform was used as the solvent. When the reaction was carried out using 3-hexyne as alkyne in THF, a red–violet solution was formed and its IR spectrum revealed terminal C≡O stretching bands at around 2000 cm^{-1} and bridged C≡O stretching bands at 1870, 1840 and 1780 cm^{-1}, which were similar to those of $[Rh_5(CO)_{15}]^-$ in THF prepared from $Na_2[Rh_{12}(CO)_{30}]$ with carbon monoxide [18, 19]. The yellow–brown reaction mixture of **1b** in THF exhibited IR bands at 2000 and 1860 cm^{-1} in the C≡O region,

TABLE 10. Effect of addition of alkylammonium chloride on the catalytic carbonylation of phenylacetylene[a]

Entry	Additive	(mmol)	Conversion (%)	Selectivity[b] (%)	**2b**:**3b**
1		(0)	100	93	54:46
2	Et_4NCl	(0.05)	75	79	77:23
3	Et_3NHCl	(0.5)	100	90	61:39

[a]Phenylacetylene (5 mmol), $Rh_6(CO)_{16}$ (3.1×10^{-3} mmol), Et_3N (0.7 mmol), H_2O (27.8 mmol), dioxane (15 ml), CO (100 atm), 80 °C, 3 h. [b]Based on phenylacetylene consumed.

which also show the presence of cluster anions like $[Rh_5(CO)_{15}]^-$ in the reaction mixture.

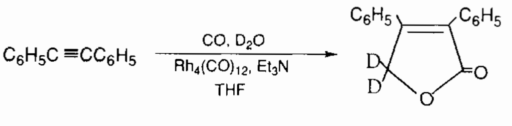
On the other hand, when chloroform was used as solvent, IR spectra of the reaction mixture of 3-hexyne as well as **1b** exhibited only absorption bands at about 2000 cm^{-1} and no bands in the range of bridged carbonyl stretching frequencies, suggesting the presence of a monomeric catalyst species. As described above, the reaction proceeded with the highest activity in chloroform in spite of its immiscibility with water and the highest initial rate was achieved when $[Rh(CO)_2Cl]_2$ was used. $[Rh(CO)_2Cl]_2$ is considered to form a monomeric species more easily than cluster complexes. So, it can be considered that the true catalyst may be monomeric and would be more stable in solvents having a lower polarity.

To confirm that the true catalyst is monomeric, a mixture of 3-hexyne, Et_3N and water was treated with $Rh_6(CO)_{16}$ in THF under an atmospheric pressure of CO at room temperature and IR spectra of the reaction solution were taken at appropriate intervals. Crystals of $Rh_6(CO)_{16}$ were dissolved and a red–violet colored clear solution was obtained after a few minutes. Its IR spectrum showed absorption bands at 2000, 1870, 1840 and 1780 cm^{-1}, indicating the presence of the $[Rh_5(CO)_{15}]^-$ anion. With the lapse of time, the color of the solution changed to dark brown and the strength of the carbonyl stretching absorptions at 1870, 1840 and 1780 cm^{-1} diminished gradually. Then, these bands disappeared almost perfectly and a new band at about 1760 cm^{-1}, indicating the formation of furanones, appeared after 24 h. The formation of a small amount of 3,4-diethyl-2(5*H*)-furanone was confirmed by GC analysis.

The above experimental results indicate that catalytic formation of furanones can take place even under atmospheric pressure of CO at room temperature although the activity is very low and the mononuclear anion would be the active species.

Mechanism

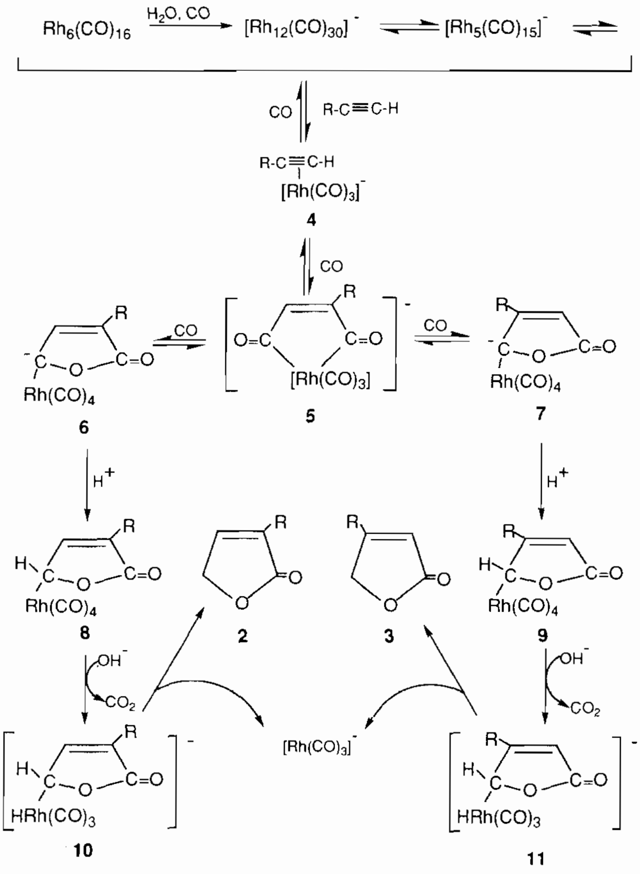
Judging from the structure, 2(5*H*)-furanone is constructed by the combination of an alkyne with one molecule of hydrogen and two molecules of carbon monoxide. We have shown in a previous paper that 5,5-dideuterio-2(5*H*)-furanone (**2a′**) was obtained when D_2O was used instead of H_2O [2b]. This fact indicates that the hydrogen atoms derive from water.



2a′ (3)

We previously proposed two possible reaction pathways for the formation of furanones in reductive carbonylation of alkynes: one is the pathway which involves a rhodium cluster as an active intermediate and the other involves a mononuclear formyl complex. But on the basis of the experimental observations described above, it is believed that the active species in the reaction would be a mononuclear anionic complex which is stabilized by coordination of an alkyne molecule. Thus, the third reaction pathway may be written as shown in Scheme 1.

In water-gas shift reaction conditions, it is well known that rhodium carbonyls are transformed to various cluster anions such as $[Rh_{12}(CO)_{30}]^{2-}$, $[Rh_5(CO)_{15}]^-]$ and so on, depending on the reaction conditions [20]. When an alkyne is present in this system, some of these cluster anions and/or neutral cluster carbonyls may give a monomeric anion (**4**) stabilized by the coordination of alkyne. Anion **4** then undergoes insertion of two molecules of carbon monoxide to give intermediate **5**, which may be in equilibrium with intermediate **6** or **7**. Then C–H bond formation by attack of a proton to the anion results in production of furanonyl complex **8** or **9**. Addition of OH^- anion to



Scheme 1. Proposed reaction path for the carbonylation of an alkyne with CO and H_2O.

a carbonyl ligand and elimination of carbon dioxide give a hydrido-σ-furanonyl anion **10** or **11**. Reductive elimination reaction of anion **10** or **11** affords furanone **2** or **3** and unsaturated anionic rhodium carbonyl species.

Many of the experimental results described above can be explained by this reaction scheme. The most important step in this scheme is thought to be the attack of a proton to the intermediate (**6** or **7**). This C—H bond formation step would be irreversible. When the counter cation of the intermediate (**6** or **7**) is replaced with a cation having no hydrogen, protonation of the intermediate (**6** or **7**) forming the furanonyl complex (**8** or **9**) would be interrupted. It seems to be for this reason that addition of $[Et_4N]^+Cl^-$ retarded the reaction although addition of $[Et_3NH]^+Cl^-$ did not depress the reaction. The role of the amine may not only be promotion of the attack of OH^- anion to the carbonyl ligand but also to contribute to stabilization of the anionic complex and to the transfer of proton to give the furanonyl complex (**8** or **9**).

The activation process of water via attack of OH^- to carbonyl ligand is considered to proceed easily, because the presence of one equivalent of water to alkyne is enough to perform the reaction smoothly and the reaction takes place in an excellent manner even in solvents which are immiscible with water.

The effect of solvents can be understood by the following consideration. The examination by IR spectra of the reaction solutions shows that a monomeric catalyst species is present in a chloroform solution, while the $[Rh_5(CO)_{15}]^-$ anion is mainly involved in a THF solution. When the reaction of **1b** was carried out using DMF as a solvent, no reaction took place (Table 4, entry 8) and the color of the reaction solution was green, suggesting the presence of more highly nucleated cluster anions, such as $[Rh_6(CO)_{15}]^{2-}$, $[Rh_7(CO)_{16}]^{3-}$ and $[Rh_{14}(CO)_{25}]^{4-}$ [20]. These observations suggest that a monomeric anion of rhodium may be stabilized in solvents having low polarity, while cluster anions of rhodium may be more stable in solvents having higher polarity under the reaction conditions. When a highly polar solvent is used, the concentration of monomeric rhodium anion would decrease and the concentration of cluster anion would increase. This may cause the lowering of the reaction activity and the selectivity.

The lack of regioselectivity in our reaction can also be understood by considering that there is no steric hindrance of the monomeric intermediate (**5**).

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