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Synthesis of 3-silyl-2(5*H*)-furanone by rhodium-catalyzed cyclocarbonylation

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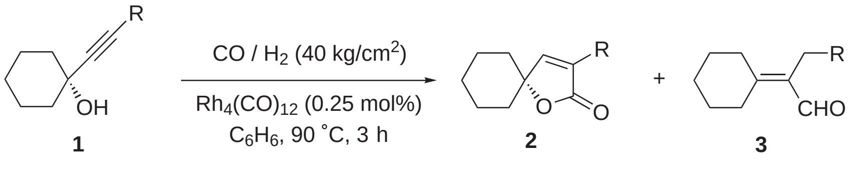
Abstract—3-Silyl-2(5*H*)-furanones are readily formed by the rhodium-catalyzed cyclocarbonylation of propargyl alcohol derivatives bearing a trialkylsilyl group on the terminal *sp*-carbon under hydroformylation conditions. The following two requirements must be satisfied for the success of this protocol; (i) the presence of a silyl group on the *sp*-carbon, and (ii) the presence of a catalytic amount of $Rh_4(CO)_{12}$. © 2001 Elsevier Science Ltd. All rights reserved.

Regio-control for the incorporation of CO into a starting substrate has been an outstanding issue since the discovery of the Roelen reaction (oxo reaction). Hydroformylation of alkene has been widely investigated, and there are many excellent papers concerning the regiochemistry of terminal alkenes.[1] However, little is known about the regio-control in hydroformylation of alkynes to give an unsaturated aldehyde because hydrogenation of the primary product proceeds under the reaction conditions.[2–4] During our project on the Rh-catalyzed selective incorporation of CO into alkynes, we explored rhodium-catalyzed silylformylation of alkynes, in which complete regio-control was realized by using a hydrosilane.[5]

As the primary target at the second stage of this project, we concentrated on the regio-control in the reaction of alkynes under hydroformylation conditions. Thus, we focussed on rhodium-catalyzed reaction of propargyl-type alcohols and found that alkynes bearing a trialkylsilyl group on the *sp*-carbon smoothly incorporate CO to form a 2(5*H*)-furanone framework. We describe here a one-pot procedure for the synthesis of 3-silyl-2(5*H*)-furanones composed of 1-substituted-3-silylpropyn-1-ols, CO, and H_2 in the presence of a catalytic amount of $Rh_4(CO)_{12}$.

First of all, a benzene solution of 1-(trimethylsilylethynyl)cyclohexan-1-ol (**1a**, R = $SiMe_3$, 1.0 mmol) and a catalytic amount of $Rh_4(CO)_{12}$ (0.25 mol% of **1a**) was heated for 3 h at 90°C under synthesis gas pressure (40 kg/cm^2, CO/H_2 = 1/1) in a glass tube contained in a stainless steel reactor. Chromatographic separation of the reaction mixture through silica gel gave two products, a spiro butenolide (**2a**)[6] and 2-cyclohexylidene-3-trimethylsilylpropanal (**3a**)[6] in 92 and 3% yields, respectively (Eq. (1)).



(1)

This result shows clearly that the selective incorporation of CO is attained on the silylated *sp*-carbon of **1a**. It should be noted that the resultant carbon–carbon double bond remained intact in both products **2a** and **3a**, although the reaction of **1a** was operated under the equal pressure of H_2 with CO. We are stimulated by this preliminary evidence because the present reaction provides a protocol for the incorporation of CO into

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Keywords: cyclocarbonylation; rhodium complex; synthesis gas; 2(5*H*)-furanone.

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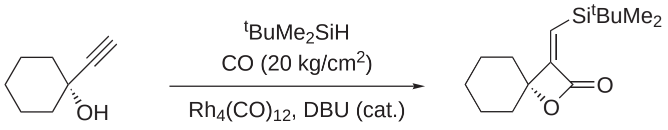
the terminal *sp*-carbon of **1b**. Selective incorporation of CO into the terminal *sp*-carbon of **1b** has been attained as shown in Eq. (2).[5b]



1b **4**

(2)

Thus, some variable factors were examined for exploring the optimal conditions. The results are summarized in Table 1. The overall carbonylation proceeded uniformly in a benzene solution under the pressure of synthesis gas from 2 to 40 kg/cm^2. The isolated yield of **2a** increased to 97% under 20 kg/cm^2 of synthesis gas (entry 2 in Table 1), while no products were obtained in the reaction under the atmosphere of CO/H_2 (entry 4 in Table 1). In sharp contrast to the result of Eq. (2), the incorporation of CO was completely suppressed by the presence of a catalytic amount of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) (entry 5 in Table 1). To the contrary, **2a** was isolated in 79% yield as the sole product despite the incomplete conversion of **1a** in the presence of 1,2,2,6,6-pentamethylpiperidine (4 mol%) (entry 6 in Table 1). Other rhodium complexes, $Rh(CO)_2(acac)$, $[Rh(cod)(dppb)]^+ClO_4^-$, and $[RhCl(CO)_2]_2$ did not exceed the efficiency of $Rh_4(CO)_{12}$ as a catalyst precursor (entries 7–9 in Table 1).

The nature of solvents affected the efficacy for the incorporation of CO. When THF was employed as a solvent instead of benzene, **2a** was obtained almost exclusively although high pressure of the synthesis gas was required for the complete conversion of **1a** (entry 10 in Table 1). Other solvents, CH_2Cl_2, CH_3CN, and EtOH, resulted in low yields of **2a** (entries 11–13 in Table 1). Yamazaki and co-workers reported the incorporation of two molecules of CO into an alkyne to give an alkoxyfuranone in the reaction using methanol as a solvent.[7] In our case, however, the corresponding product was not detected at all even in the reaction using ethanol as a solvent.

The presence of a silyl group on the *sp*-carbon seems to be crucial for smooth incorporation of CO in the present-type cyclocarbonylation. Alkynols bearing *tert*-$BuMe_2Si$ (**1c**), Et_3Si (**1d**), and Me_2PhSi (**1e**) as R reacted uniformly to give **2**[6] (entries 14–16 in Table 1), while other alkynols (R = H, phenyl, *n*-butyl, and methoxycarbonyl) resulted in no reaction with recovery of the starting materials under similar conditions. In contrast to Rh-catalyst, a similar transformation catalyzed by $Pd_2(dba)_3 \cdot CHCl_3$ is free from this constraint.[8] Our method, however, makes it possible to shorten appreciably the time required for completion in the reaction of specific substrates.

Table 1. Cyclocarbonylation of **1**[a]

Entry	Alkyne (**1**)		Pressure of CO/H_2 (kg/cm^2)	Solvent	Time (h)	Yield (%)[b]		Recovery (%)
		R				**2**	**3**	**1**
1	**1a**	Me_3Si	40	C_6H_6	3	92	3	0
2	**1a**	Me_3Si	20	C_6H_6	3	97	<1	0
3	**1a**	Me_3Si	2	C_6H_6	13	89	3	8
4	**1a**	Me_3Si	1	C_6H_6	6	0	0	>90
5[c]	**1a**	Me_3Si	20	C_6H_6	3	0	0	>90
6[d]	**1a**	Me_3Si	20	C_6H_6	3	79	0	11
7[e]	**1a**	Me_3Si	20	C_6H_6	3	37	0	62
8[f]	**1a**	Me_3Si	20	C_6H_6	3	15	0	85
9[g]	**1a**	Me_3Si	20	C_6H_6	3	0	0	>90
10	**1a**	Me_3Si	40	THF	3	99	<1	0
11	**1a**	Me_3Si	20	CH_2Cl_2	3	27	0	61
12	**1a**	Me_3Si	20	CH_3CN	3	14	0	74
13	**1a**	Me_3Si	20	EtOH	3	46	0	40
14	**1c**	$^tBuMe_2Si$	20	C_6H_6	3	92	6	0
15	**1d**	Et_3Si	20	C_6H_6	3	77	3	0
16	**1e**	Me_2PhSi	40	C_6H_6	3	79	0	0

[a] Reactions were carried out on a 1.0 mmol scale of **1** at 90°C using $Rh_4(CO)_{12}$ (0.25 mol%) as a catalyst under synthesis gas pressure ($CO/H_2 = 1/1$).

[b] Isolated yields.

[c] 5 mol% of DBU was added.

[d] 4 mol% of 1,2,2,6,6-pentamethylpiperidine was added.

[e] $Rh(CO)_2(acac)$ (1.0 mol%) was used as a catalyst.

[f] $[Rh(cod)(dppb)]^+ClO_4^-$ (1.0 mol%) was used as a catalyst.

[g] $[RhCl(CO)_2]_2$ (0.5 mol%) was used as a catalyst.

Table 2. Rhodium-catalyzed cyclocarbonylation of **5**[a]

Entry	Alkynol (**5**)			Solvent	CO/H_2 (kg/cm^2)	Yield (%)[b]		Ratio
		R^1	R^2			**6**[6]		**6**:**7**[c]
1	**5a**	-$(CH_2)_4$-		THF	40[d]	**6a**	82	95:5
2	**5b**	-$(CH_2)_6$-		THF	40	**6b**	95	99:1
3	**5c**	Et	Et	C_6H_6	20	**6c**	83	98:2
4	**5d**	Me	Ph	C_6H_6	20	**6d**	88	97:3
5	**5e**	Ph	Ph	C_6H_6	20	**6e**	85	94:6
6	**5f**	H	Oct	C_6H_6	40	**6f**	67	90:10
7	**5f**	H	Oct	THF	40	**6f**	72	96:4
8	**5g**	H	^{i}Pr	C_6H_6	40	**6g**	74	93:7
9	**5g**	H	^{i}Pr	THF	40	**6g**	76	93:7
10	**5h**	H	Ph	C_6H_6	40	**6h**	76[e]	88:12
11	**5h**	H	Ph	THF	40	**6h**	95[e]	96:4
12	**5i**	H	CH=CHPh	C_6H_6	40	**6i**	0[f]	–

[a] Reactions were carried out on a 1.0 mmol scale of **5** containing a $Rh_4(CO)_{12}$ (0.25 mol%) for 3 h at 90°C under synthesis gas pressure ($CO/H_2 = 1/1$).

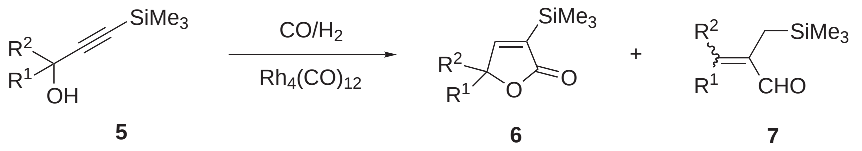
[b] Isolated yields.

[c] The ratio was estimated from NMR spectrum of a crude mixture.

[d] The reaction was carried out for 12 h.

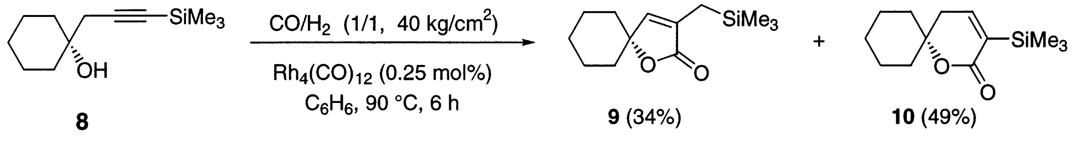
[e] The yield was estimated from NMR spectrum after a bulb-to-bulb distillation of a crude mixture.

[f] **5i** was recovered intact.

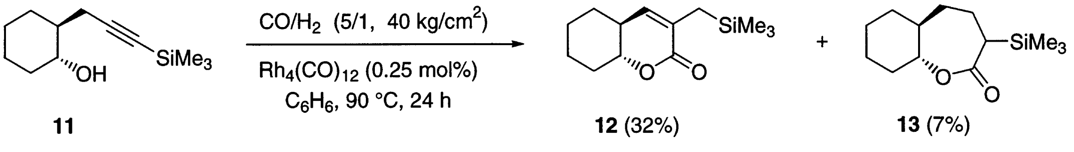


(3)

Next, various types of propargyl alcohol (**5**) were subjected to the present carbonylation in order to clarify the scope and limitation of the method. The results are summarized in Table 2. Alkynols bearing two substituents on the propargyl position (**5a**–**e**) gave the corresponding furanones[6] in high yields and high regioselectivity (entries 1–5 in Table 2). Less substituted ones resulted in a slight decrease of the selectivity for **6** (entries 6, 8, and 10 in Table 2) in addition to the requirement of relatively high pressure of synthesis gas (40 kg/cm^2) for the complete conversion of **5**. The yield and the selectivity of **6f**–**h**[6] were remarkably improved by replacing benzene with THF as the solvent. In particular, the yield of **6h** increased to 95% (entries 7, 9, and 11 in Table 2). In sharp contrast to these results, a styryl group on the propargyl carbon inhibited carbonylation under our conditions (entry 12 in Table 2), although the incorporation of CO was reported in the reaction of 1,4-diphenylbut-1-en-3-yne.[9]



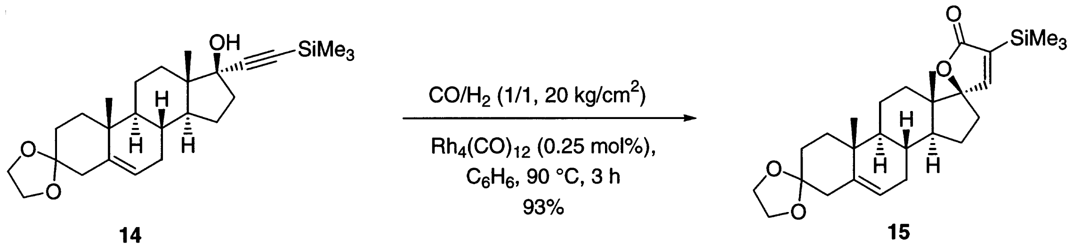
(4)



(5)

The position of the hydroxy group in the starting substrates also affected the reaction path. Two types of lactone were isolated as major products in the carbonylation of silylated alkynes **8** and **11**, respectively, under analogous conditions (Eqs. (4) and (5)). These results imply that the rhodium species cannot kinetically differentiate two *sp*-carbons of alkynes, **8** and **11**, under the conditions. Therefore, intervention of a thermodynamically controlled step should be assumed for elucidation of the remarkable high regio-selectivity in the reactions of **1** and **5**.

Our protocol was also applied to a steroidal propargyl alcohol **14** to form a spiro lactone **15** as the sole product (93%) (Eq. (6)). In this reaction, the olefinic unit of **14** remained intact after the carbonylation step. A similar transformation has been attained through hydroformylation of an alkynol part in which an oxidation step was inevitably required for the dehydrogenation from the lactol intermediate.[10]



14 **15** (6)

In summary, we have developed a new method for the transformation of propargyl alcohols to form 2(5*H*)-furanones bearing a trialkylsilyl group, in which $Rh_4(CO)_{12}$ is the most suitable as a catalyst under hydroformylation conditions. We have described the scope and limitation of this protocol and demonstrated the successful result for ethisterone. The trialkylsilyl group contained in the resultant furanones would become an important clue for various transformations.[11]

Acknowledgements

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6. All these compounds were identified by ^1H NMR, ^{13}C NMR and IR spectra. All new compounds gave satisfactory combustion analyses. For example, **2a**: white needles from hexane (mp 117.2–117.5°C). IR (CCl_4): 1751 ($\nu_{C=O}$), 1597 ($\nu_{C=C}$), 1252 (ν_{Si-C}) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.23 (s, 9H, Si-$(CH_3)_3$), 1.25–1.79 (m, 10H, -$(CH_2)_5$-), 7.45 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: −2.08 ($SiCH_3$), 22.50 (-$(CH_2)_5$-), 24.63 (-$(CH_2)_5$-), 34.55 (-$(CH_2)_5$-), 88.21 (OC), 132.60 (=CSi), 168.12 (=CH), 174.77 (C=O). Anal. calcd for $C_{12}H_{20}O_2Si$: C, 64.24; H, 8.98. Found: C, 64.30; H, 9.11.
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