Extremely Regioselective Intramolecular Silylformylation of Alkynes

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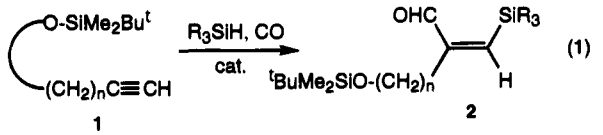
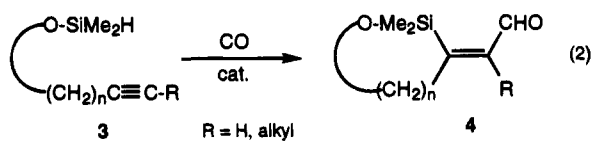
The intermolecular silylformylation of alkynes catalyzed by Rh or Co–Rh complexes, which gives the corresponding β-formylvinylsilanes in high yields, has been studied extensively in recent years.[1-3] Silylcarbocyclizations (SiCACs) of alkenynes,[4] diynes,[4,5] aldehydes,[6] and alkynals[7] have also been investigated. In the silylformylation of 1-alkynes, the reaction gives 1-silyl-2-formyl-1-alkenes with complete regioselectivity.[1-3] This markedly high regioselectivity is useful, but it is more useful if the regioselectivity of the reaction can be controlled so that 3-silyl-2-alken-1-als become accessible. The reaction of simple internal alkynes, however, is virtually nonselective, giving a mixture of regioisomers.[2a] Accordingly, we investigated the intramolecular version of the silylformylation of 1-alkynes and internal alkynes by introducing a dimethylsiloxy, i.e., HMe_2SiO, moiety as the directing group. We will describe here our successful preliminary results on the intramolecular silylformylation of ω-(dimethylsiloxy)-*i*-alkynes catalyzed by Rh and Rh-Co complexes, which proceeds with complete regioselectivity, giving 3-*exo*-(formylmethylene)oxasilacycloalkanes with or without an alkyl substituent at the *exo*-methylene carbon, which are equivalent to ω-siloxy-(*i*+1)-silyl-*i*-alken-*i*-als, in excellent yields.

When an ω-(*tert*-butyldimethylsiloxy)-1-alkyne (**1**) is employed as the substrate for the standard intermolecular silylformylation, the reaction should yield the corresponding ω-(*tert*-butyldimethylsiloxy)-2-formyl-1-silylalkene (**2**). For example, the reaction of 4-*tert*-butyldimethylsiloxy-1-butyne (**1a**) with diphenylmethylsilane (1.1 equiv) catalyzed by $(^tBuNC)_4RhCo(CO)_4$ (0.2 mol %) in toluene at 60 °C and 10 atm of carbon monoxide for 14 h gave (*Z*)-4-(*tert*-butyldimethylsiloxy)-2-formyl-1-(diphenylmethylsilyl)-1-butene (**2a**) in 82% isolated yield (eq 1).[8]



(1)

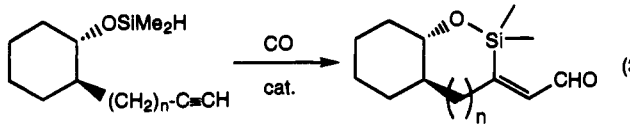


(2)

We introduced a ω-dimethylsiloxy moiety to 1-alkynes and internal alkynes as the directing group. These ω-(dimethylsiloxy)alkynes (**3**) were readily prepared by reacting *i*-alkyn-1-ols with 1,1,3,3-tetramethyldisilazane in the presence of a catalytic amount of ammonium chloride.[9] The reactions of ω-(dimethylsiloxy)-*i*-alkynes (**3**) were carried out in the presence of $(^tBuNC)_4RhCo(CO)_4$,[10] $Rh_2Co_2(CO)_{12}$,[11] or $Rh(acac)(CO)_2$ (0.5 mol %) in toluene at 60–70 °C for 3–14 h to give the corresponding 3-*exo*-(formylmethylene)oxasilacycloalkanes (**4**) in excellent yields (eq 2).[12] The products **4** were isolated by bulb-to-bulb distillation: **4** are unstable on a silica gel column.[12] Results are summarized in Table 1.

As Table 1 shows, the reactions of ω-(dimethylsiloxy)-1-alkynes, **3a** and **3b**, give the corresponding silylformylation products, **4a** and **4b**, respectively, which are equivalent to ω-siloxy-3-silyl-2-alken-1-als, i.e., the regioselectivity is completely reversed from that of the standard silylformylation as we predicted. The reactions of internal alkynes, i.e., ω-(dimethylsiloxy)-*i*-alkynes, **3c** and **3d**, proceed cleanly to give **4c** and **4d**, respectively, as the sole product.

The intramolecular silylformylation is applicable to cyclic systems. The reaction of *O*-(dimethylsilyl)-2-ethynyl-1-cyclohexanol (**5**) or *O*-(dimethylsilyl)-2-(2-propynyl)-1-cyclohexanol (**6**) catalyzed by $(^tBuNC)_4RhCo(CO)_4$ proceeded smoothly at 65 °C and 10 atm of carbon monoxide to give the corresponding exocyclic 3-silyl-2-alken-1-al, **7** or **8**, as the sole stereo- and regioisomer in excellent yields (eq 3). Results are shown in Table 1.



(3)

5: n = 0
6: n = 1
7: n = 0
8: n = 1

As catalysts for the intramolecular silylformylation, we have examined the efficacy of $(^tBuNC)_4RhCo(CO)_4$, $Rh_2Co_2(CO)_{12}$, $Rh(acac)(CO)_2$, and $Rh_4(CO)_{12}$. As Table 1 shows, Rh–Co mixed-metal complex $(^tBuNC)_4RhCo(CO)_4$ gives the best results for all substrates examined. We have observed that the reactions

† State University of New York at Stony Brook.
‡ Nagoya University.

(1) (a) Ojima, I.; Ingallina, P.; Donovan, R. J.; Clos, N. *Organometallics* **1991**, *10*, 38. (b) Ojima, I.; Donovan, R. J.; Eguchi, M.; Shay, W. R.; Ingallina, P.; Korda, A.; Zeng, Q. *Tetrahedron* **1993**, *49*, 5431. (c) Ojima, I.; Donovan, R. J.; Ingallina, P.; Clos, N.; Shay, W. R.; Eguchi, M.; Zeng, Q.; Korda, A. *J. Cluster Sci.*, **1992**, *3*, 423–438. (d) Ojima, I.; Zhang, Z.; Korda, A.; Ingallina, P.; Clos, N. In *New Science in Homogeneous Transition Metal Catalyzed Reactions*; Moser, W. R., Ed.; Advances in Chemistry, No. 230, American Chemical Society: Washington, DC, 1992; Chapter 19, pp 277–296.

(2) (a) Matsuda, I.; Ogiso, A.; Sato, S.; Izumi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2332. (b) Matsuda, I.; Ogiso, A.; Sato, S. *J. Am. Chem. Soc.* **1990**, *112*, 6120. (c) Matsuda, I.; Sakakibara, J.; Nagashima, H. *Tetrahedron Lett.* **1991**, *32*, 7431.

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(4) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580.

(5) (a) Ojima, I.; Fracchiolla, D. A.; Donovan, R. J.; Banerji, P. *J. Org. Chem.* **1994**, *59*, 7594. (b) Matusda, I.; Ishibashi, H.; Ii, N. *Tetrahedron Lett.* **1995**, *36*, 241.

(6) Wright, M. E.; Cochran, B. B. *J. Am. Chem. Soc.* **1993**, *115*, 2059.

(7) Ojima, I.; Tzamarioudaki, M.; Tsai, C.-Y. *J. Am. Chem. Soc.* **1994**, *116*, 3643.

(8) The reaction was run following the standard procedure[1b] using **1a** (0.50 mmol) and diphenylmethylsilane (0.55 mmol) in the presence of $(^tBuNC)_4RhCo(CO)_4$ (0.2 mol %) in toluene (3.0 mL) at 60 °C and 10 atm of carbon monoxide for 14 h. Column chromatography of the reaction mixture on silica gel gave (*Z*)-4-(*tert*-butyldimethylsiloxy)-2-formyl-1-(diphenylmethylsilyl)-1-butene (**2a**) in 82% yield.

(9) Tamao, K.; Nakagawa, Y.; Arai, H. Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 3712. As an example, the preparation of 4-(dimethylsiloxy)-1-butyne (**3a**) is described: In a 25 mL round-bottom flask, 3-butyn-1-ol (1.00 g, 14.3 mmol) and ammonium chloride (19.8 mg, 0.37 mmol) were introduced. To this mixture was added 1,1,3,3-tetramethyldisilazane (2.5 mL, 14.2 mmol) dropwise via syringe under nitrogen. The reaction mixture was stirred overnight. The excess of 1,1,3,3-tetramethyldisilazane was removed under reduced pressure, and the residue was submitted to bulb-to-bulb distillation to give **3a** (1.80 g, 98% yield) as a colorless oil.

(10) Ojima, I.; Clos, N.; Donovan, R. J.; Ingallina, P. *Organometallics* **1991**, *10*, 3211.

(11) (a) Martinengo, S; Chini, P.; Albano, V. G.; Cariati, F. *J. Organomet. Chem.* **1973**, *59*, 379. (b) Horváth, I. T.; Bor, G.; Garland, M.; Pino, P. *Organometallics* **1986**, *5*, 1441.

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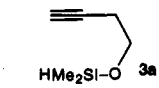
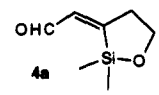
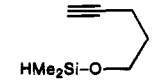
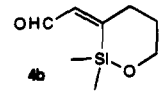
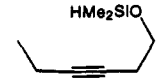
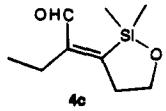
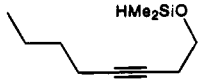
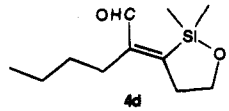
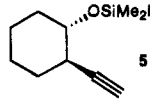
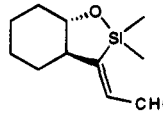
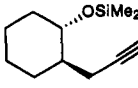
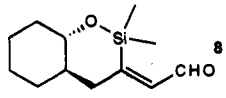
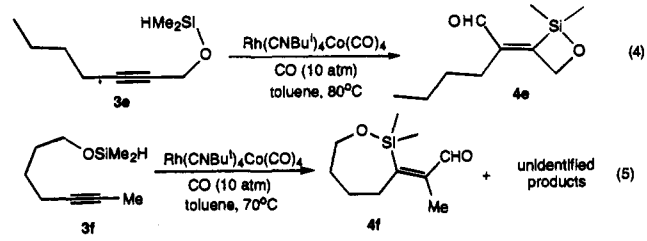
Table 1. Intramolecular Silylformylation of ω-(Dimethylsiloxy)alkynes[a]

Entry	ω-HSiMe$_2$O-alkyne	Catalyst	Temp. (°C)	Time (h)	Product	Yield (%)[b]
1		(^{t}BuNC)$_4$RhCo(CO)$_4$	70	14		89 (42)
2		Rh$_2$Co$_2$(CO)$_{12}$	70	18		46
3	HMe$_2$Si–O 3a	Rh(acac)(CO)$_2$	70	16	4a	62
4		(^{t}BuNC)$_4$RhCo(CO)$_4$	70[c]	23		81
5	HMe$_2$Si–O 3b	Rh(acac)(CO)$_2$	70[c]	14	4b	73
6	 3c	Rh$_4$(CO)$_{12}$, Et$_3$N	85[d]	2	 4c	77 (51)
7	 3d	(^{t}BuNC)$_4$RhCo(CO)$_4$	60	14		99 (66)
8		Rh$_2$Co$_2$(CO)$_{12}$	60	3		84
9		Rh(acac)(CO)$_2$	60	3		93
10		Rh$_4$(CO)$_{12}$, Et$_3$N	85[d]	3.5	4d	69
11	 5	(^{t}BuNC)$_4$RhCo(CO)$_4$	65	14		100 (69)
12		Rh$_2$Co$_2$(CO)$_{12}$	65	3		92
13		Rh(acac)(CO)$_2$	65	3	7	94
14	 6	(^{t}BuNC)$_4$RhCo(CO)$_4$	65	14		99 (73)
15		Rh$_2$Co$_2$(CO)$_{12}$	65	3		80
16		Rh(acac)(CO)$_2$	65	3	8	96

[a] Reactions were run with ω-(dimethylsiloxy)alkyne (0.50 mmol) and a catalyst (2.5×10^{-3} mmol) in dry toluene (3.0 mL) in a 5 mL Pyrex reaction vessel under carbon monoxide (10 atm) using a 300 mL stainless steel autoclave unless otherwise noted. [b] GC yield. The value in parentheses is isolated yield after bulb-to-bulb distillation. [c] The reaction was performed in 15 mL of dry toluene under 50 atm of carbon monoxide. [d] The reaction was run using 2.76 mmol of ω-(dimethylsiloxy)alkyne, 7.3×10^{-3} mmol of catalyst, and 2.91 mmol of triethylamine in 13 mL of dry benzene under 20 atm of carbon monoxide.

using Rh$_4$(CO)$_{12}$ are often slow and give other side reaction products. The rate and selectivity appear to be improved in the presence of triethylamine.

The reaction of 3-(dimethylsiloxy)-1-propyne (**3**, $n = 1$, R = H) did not proceed at all regardless of the catalyst used. On the contrary, the reaction of 1-(dimethylsiloxy)-2-heptyne (**3e**) catalyzed by (^{t}BuNC)$_4$RhCo(CO)$_4$ gave 3-*exo*-(1-formylpentylid-1-ene)-1-oxa-2-silacyclobutane (**4e**) in 50–60% yield (eq 4). However, the stability of this product (**4e**) is low, and thus even isolation by means of bulb-to-bulb distillation is problematic in obtaining reproducible results. Accordingly, optimization of isolation conditions is necessary. The reaction of 7-(dimethylsiloxy)-2-heptyne (**3f**) catalyzed by (^{t}BuNC)$_4$RhCo(CO)$_4$ gave a mixture of not yet fully identified products (eq 5). Nevertheless, a small amount of **4f** was detected by ^{1}H NMR (aldehyde proton appears at δ 9.67), and GC–MS analysis showed the molecular ion peak (*m/z* 198) and ($M^+ - 15$) peak (*m/z* 183). Optimization for selective formation of **4f** is in progress.



Further studies on the scope and limitations as well as applications of extremely regioselective directed silylformylation are actively underway.

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Supplementary Material Available: General experimental procedures for the extremely regioselective intramolecular silyl formylation of **1** and characterization data for new compounds **3a–e**, **5**, **6**, **4a–e**, **7**, and **8** (5 pages). This material is contained in many libraries on microfiche, immediately follow this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(12) General procedure: To a 5 mL round-bottom flask containing a catalyst (2.5×10^{-3} mmol) and a stirring bar was added 1.0 mL of toluene under carbon monoxide pressure. A solution of 1-(dimethylsiloxy)alkyne (0.50 mmol) in 2.0 mL of toluene was added to the reaction flask, which was then placed in a 300 mL stainless steel autoclave. Carbon monoxide was introduced to substitute the remaining air. After the carbon monoxide pressure was adjusted to 10 atm at room temperature, the autoclave was immersed into an oil bath and stirred magnetically at 65–70 °C for 3–24 h. The reaction time required for completion was dependent on the nature of the catalyst and the substrate used. Then, carbon monoxide was carefully released and the reaction mixture was submitted to GC analysis. The GC yields were determined by using undecane as the internal standard. The solvent was removed under reduced pressure, and the intramolecular silylformylation product was isolated by bulb-to-bulb distillation.