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Desymmetrization of 4-Dimethylsiloxy-1,6-heptadiynes through Sequential Double Silylformylation

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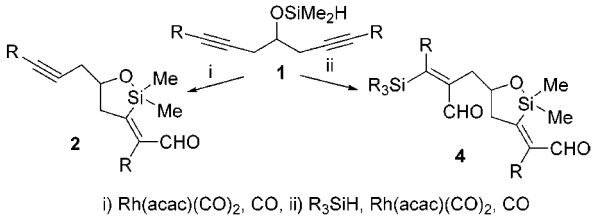
ABSTRACT



i) $Rh(acac)(CO)_2$, CO, ii) R_3SiH, $Rh(acac)(CO)_2$, CO

Desymmetrization of dimethylsilyloxyalkadiynes (1) by Rh-catalyzed intramolecular silylformylation affords 5-*exo*-(formylmethylene)-oxasilacyclopentanes 2 in high yields. Novel sequential double silylformylation of 1a also provides desymmetrization, giving 3-(3-silyl-2-formylprop-2-enyl)-5-*exo*-(formylmethylene)oxasilacyclopentanes 4 in excellent yields. Reduction of 2a and 4 with $NaBH_4$ gives the corresponding 5-*exo*-(hydroxymethylmethylene)oxasilacyclopentanes 3a and 5, respectively.

Silylformylation of alkynes catalyzed by Rh and Co−Rh complexes has been extensively studied in the past decade and provides a powerful method for the regio- and stereoselective syntheses of β-formylvinylsilanes.[1−6] The reaction has been applied to the efficient synthesis of pyrrolizidine alkaloids and other organic syntheses.[1d,2b,7,8] The silylformylation of 1-alkynes gives (*Z*)-1-silyl-2-formyl-1-alkenes with complete regio- and stereoselectivity.[1−4] However, this means that it is practically impossible to obtain the products with opposite regiochemistry, i.e, (*Z*)-2-silyl-1-formyl-1-alkenes. The control of regioselectivity is, however, difficult for the reaction of simple internal alkynes.[2] To solve this problem, the intramolecular silylformylation of 1-alkynes and internal alkynes has been successfully developed by introducing a dimethylsiloxy, i.e., HMe_2SiO, moiety as the directing group.[5] A similar reversal of selectivity was achieved by introducing a $HSiR_2$ moeity to the alkyl terminal carbon of alkynes.[6] Intramolecular silylformylation of ω-hydrosiloxyalkenes has also been developed using $Rh(acac)(CO)_2$ as catalyst under very high pressure of CO (68 atm).[9] We

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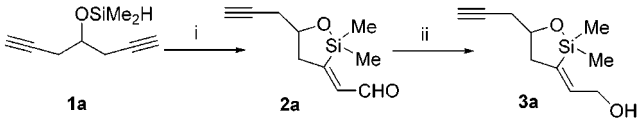
describe here our preliminary results on the successful desymmetrization of dimethylsiloxyalkadiynes based on Rh-catalyzed silylformylation, as well as a novel sequential double silylformylation protocol.

Desymmetrization of Dimethylsiloxyalkadiynes. Intramolecular silylformylation of 4-dimethylsiloxy-1,6-heptadiyne (**1a**) catalyzed by $Rh(acac)(CO)_2$ (0.5 mol %) in toluene (0.072 M) at 25 °C and 10 atm of CO proceeded smoothly to give 5-*exo*-(formylmethylene)oxasilacyclopentane **2a** in 98% yield (Scheme 1). When the reaction was

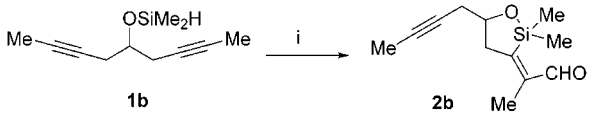
Scheme 1. Desymmetrization of 4-Dimethylsiloxy-1,6-heptadiyne (**1a**) by Rh-Catalyzed Intramolecular Silylformylation[a]



[a] (i) $Rh(acac)(CO)_2$, CO (10 atm), toluene, rt, 16 h, 98%; (ii) $NaBH_4$, MeOH, O °C, 50 min, 70%.

carried out under 1−5 atm of CO, intramolecular hydrosilylation of **1a** took place in addition to the desired silylformylation. Since **2a** was found to be unstable for purification through a silica gel column, it was reduced to the corresponding alcohol **3a** using $NaBH_4$ in methanol (70% isolated yield after purification though silica gel column). In a similar manner, the reaction of 5-dimethylsiloxy-2,7-nonadiyne (**1b**) at 60 °C and 20 atm of CO cleanly gave the corresponding intramolecular silyformylation product **2b** in 82% isolated yield, which was stable for chromatographic purification on silica gel (Scheme 2).

Scheme 2. Desymmetrization of the 5-Dimethylsiloxy-2,7-nonadiyne (**1b**) by Rh-Catalyzed Intramolecular Silylformylation[a]

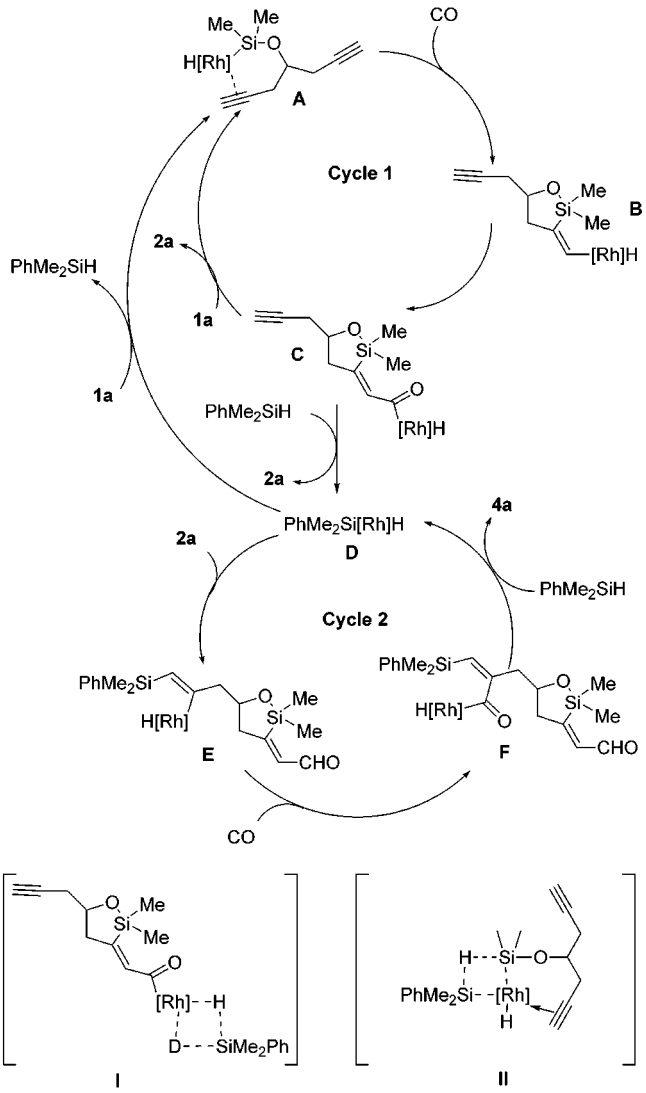


[a] (i) $Rh(acac)(CO)_2$, CO (20 atm), toluene, 60 °C, 16 h, 82%.

These reactions have achieved the desymmetrization of siloxyalkadiynes to give highly functionalized useful synthetic intermediates **2a** and **2b**, which can readily be further manipulated at the unreacted acetylene moiety as well as the α,β-unsaturated aldehyde moiety. It is obvious that after appropriate reduction of the aldehyde moiety the subsequent Tamao oxidation[10] of these compounds would lead to the formation of the corresponding 1,3,5-triols.[11]

Desymmetrization of 1a via Sequential Double Silylformylation. If the intramolecular silylformylation of **1a** is much faster than the intermolecular reaction, the sequential double silylformylation of **1a** should take place in the presence of 1 equiv of a hydrosilane to give 3-(3-silyl-2-formylprop-2-enyl)-5-*exo*-(formylmethylene)-oxasilacyclopentane **4** (Table 1). In fact, the reaction of **1a** catalyzed by

Scheme 3. Mechanism of the Double Silylformylation of **1a** with $PhMe_2SiH$



$Rh(acac)(CO)_2$ (0.5 mol %) in the presence of $HSiMe_2Ph$ or $HSiEt_3$ at 25 °C and 10 atm of CO proceeded smoothly to give **4** (R_3Si = (a) $PhMe_2$; (b) Et_3Si) in quantitative yield. The reaction using a bulky and less reactive hydrosilane, $HSiMe_2{}^tBu$, required 50 °C for 24 h to complete, affording **4c** in excellent yield. Results are summarized in Table 1.

To establish the mechanism of this double silylformylation, the reaction of **1a** in the presence of the most reactive silane (Me_2PhSiH) was monitored by ^1H NMR. The integration of

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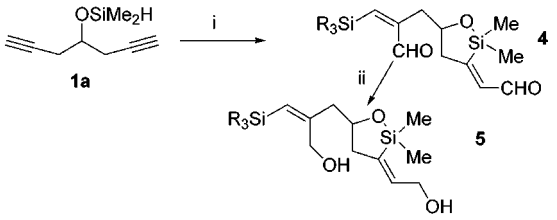
Table 1. Sequential Double Silylformylation of 4-Dimethylsilyl-1,6-heptadiyne **1a**[a]



	hydrosilane	conditions	**4** (%)[b]	**5** (%)[c]
a	$PhMe_2SiH$	rt, 8 h	100	56
b	Et_3SiH	rt, 18 h	100	74
c	$^tBuMe_2SiH$	50 °C, 24 h	98	62

[a] Conditions: (i) R_3SiH, $Rh(acac)(CO)_2$, CO (10 atm), toluene; (ii) $NaBH_4$, MeOH, 0 °C. [b] GC yield using methylene chloride as external standard. [c] Isolated yield.

the aldehyde signals at δ 9.5 (d, $^3J = 4.12$ Hz, intramolecular silylformylation) and δ 9.7 (s, intermolecular silylformylation) as well as the integration of the signal corresponding to the unreacted terminal alkyne at δ 2.0 (t, $^4J = 2.5$ Hz) allowed an accurate determination of the composition of the reaction mixture at a given time. It was found that during the first 2 h of the reaction, the intramolecular silylformylation proceeded exclusively, affording **2a**. Once the intramolecular reaction had completed ($t \geq 2$ h), the intermolecular reaction took place to give **4a**. Thus, this transformation can be called "sequential double silylformylation".

To look into the mechanism of the unique sequential double silylformylation process, a labeling experiment was performed using $PhMe_2SiD$. Then, rather unexpectedly, the deuterium incorporation to both aldehyde moieties was observed (35% to the aldehyde arising from the intramolecular silylformylation and 65% to that from the intermolecular reaction). This scrambling clearly indicates that H−D exchange takes place at a certain intermediate in the catalytic cycle. We propose a catalyst cycle that can accommodate the observed results in Scheme 3. Cycle 1 depicts the intramolecular reaction, and cycle 2 the intermolecular reaction. It is very likely that the observed H−D exchange takes place at the intermediate **C**, where $PhMe_2SiD$ can react with **C** instead of **1a** through σ-bond metathesis (see transition state **I**) to form $PhMe_2SiH$ and deuterated **2a** after reductive elimination. When $PhMe_2SiH$ thus generated is involved in cycle 2, it leads to the formation of nondeuterated aldehyde moiety. When the concentration of **1a** is sufficient enough, the resulting $PhMe_2Si[Rh]H$ does not react with the unreacted acetylene moiety of **2a** to go into cycle 2 but rather reacts with **1a** to regenerate **A** and go back to cycle 1 through σ-bond metathesis (see transition state **II**). This is due to the fact that **1a** has a much stronger affinity to Rh-catalyst species than $PhMe_2SiH(D)$ because of its two acetylene groups. It is reasonable to assume that $PhMe_2SiH(D)$ would start competing with **1a** when the concentration of **1a** is decreased as the intramolecular reaction proceeds.

In conclusion, the desymmetrization of dimethylsilyloxyalkadiynes **1** by Rh-catalyzed intramolecular silylformylation and novel sequential double silylformylation of **1a** was successfully achieved to afford highly functionalized useful synthetic intermediates, oxasilacyclopentanes **2** and **4**.

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Supporting Information Available: The characterization datas of compounds **2**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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