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A Simple Method To Polyhydroxylated Olefinic Molecules Using Ring-Closing Olefin Metathesis

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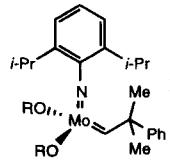
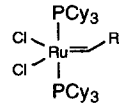
Abstract: This paper describes the ring-closing metathesis of silyl ether connected dienes using molybdenum and ruthenium alkylidene catalysts. The cyclizations proceed to afford the corresponding cyclic silyloxy olefins in good to excellent yields. Subsequent oxidative ring cleavage yields highly functionalized olefins. © 1997 Elsevier Science Ltd.

Following the initial reports,[1] catalytic ring-closing metathesis (RCM) has emerged as a powerful strategy for organic synthesis and has been extensively employed in the synthesis of a wide variety of complex molecules with multiple functionality.[2] This has been possible largely due to the development of the well-defined and highly efficient transition metal alkylidenes (for example, **1**[3] and **2a-b**[4]). Among the recent applications to synthetic organic chemistry, reports have disclosed the very useful transformation of cyclized adducts into more valuable acyclic molecules.[5]



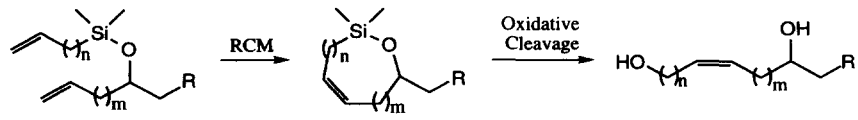
1: R CMe$(CF_3)_2$



2a: R = $CHCPh_2$
2b: R = Ph

To explore a new synthetic strategy for highly functionalized molecules, we envisioned that RCM of silicon-connected dienes and subsequent oxidative ring cleavage would provide a series of acyclic poly hydroxy olefins as illustrated in Scheme 1.

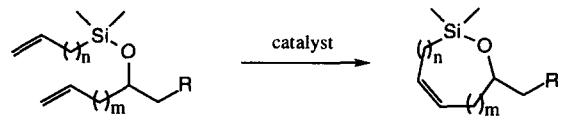
Scheme 1



Silicon was chosen as a temporary connecting atom between two olefins because its derivatives could be easily prepared and the silicon atom is readily removed under oxidative conditions.[6]

Acyclic silyl ether dienes (**3**-**10**) were prepared in three steps: i) benzylation of glycidol, ii) epoxide opening with the olefinic Grignard reagent, and iii) silylation of the secondary alcohol with the corresponding alkenyl chlorodimethylsilanes.[7] Cyclization reactions were conducted for a series of silicon-connected dienes as summarized in Table 1.[8] Most silyl ether dienes tested in this study were efficiently cyclized at room temperature within a few hours, producing the corresponding cyclic olefins in good to excellent yields with either the Mo- or Ru-catalyst depending on the type of dienes.

Table 1. Ring Closing Metathesis of Acyclic Silicon Connected Dienes



entry	diene (m, n, R)	catalyst (mol%)	solvent[a]	time (h)	yield (%)[b]
1	**3** (0, 1, CH_3)	**2b** (2)	CH_2Cl_2	1	95
2	**4** (1, 0, OCH_2Ph)	**1** (3)	C_6H_6	0.5	84
3	**5** (1, 1, OCH_2Ph)	**2b** (3)	CH_2Cl_2	3	88
4	**6** (1, 2, OCH_2Ph)	**2b** (3)	CH_2Cl_2	3	93
5	**7** (2, 0, OCH_2Ph)	**1** (5)	C_6H_6	5	91
6	**8** (2, 1, Cl)	**2** (5)	CH_2Cl_2	1	90
7	**9** (2, 1, OCH_2Ph)	**2b** (5)	CH_2Cl_2	3	96
8[c]	**9** (2, 1, OCH_2Ph)	**2b** (5)	CH_2Cl_2	3	91
9	**10** (4, 1, OCH_2Ph)	**1** (5)	C_6H_6	1	73

[a] The reactions were conducted at room temperature and the concentration of each reaction was 0.05 M except in the case of entry 8. [b] Isolated yields. [c] The concentration of the reaction was 0.15 M.

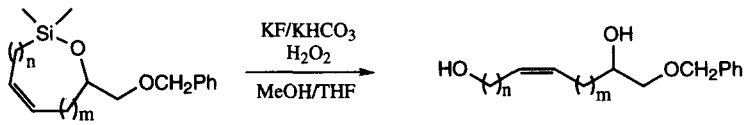
While RCM of allylsilyloxy dienes were quantitatively effected with Ru-catalyst **2b** (2-5 mol%, CH_2Cl_2) to afford the medium-sized cyclic olefins, Mo-complex **1** (5 mol%) was

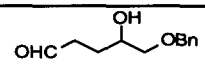
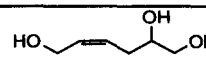
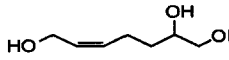
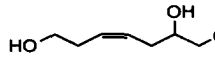
observed to be more efficient catalyst (in benzene) than Ru-complex **2** for the cyclization of vinylsilyl ether dienes **4** and **7**, presumably by the fact that latter type of olefin is sterically more demanding than the allylsilyloxy olefins and, therefore, require a metathesis catalyst less sensitive to steric bulks near the reaction center (entries 2, 5). These illustrate the first examples of RCM of vinylsilyl containing olefins. Cyclization of (3-butenyl)silyl ether diene **10** to form a 10-membered ring product also proceeded more efficiently with the Mo-catalyst **1** (entry 7).

The essentially quantitative cyclization of diene **8** and **9** with Ru-catalyst **2b** is especially noteworthy in that the cyclized product is a 8-membered ring and the efficiency of this conversion does not require high dilution conditions commonly used for the formation of 8-membered rings.[9] Even though it can be envisioned that the β-effect of silicon may result in the initial rate enhancement of a newly forming alkylidene, it is not straightforward at present to explain the high reactivity of this type of diene.

Following the successful formation of various cyclic silyl ethers, we attempted subsequent oxidative cleavage of the cycloalkenes. As seen in Table 2, ring cleavage using the oxidative conditions developed by Tamao[10] efficiently afforded the corresponding *cis*-olefinic dihydroxy compounds (hydroxyaldehyde in case silyl ether ring) in good to excellent yields.[11]

Table 2. Oxidative Cleavage of Cyclic Silyl Ether Olefins



(m, n)	product	yield	(m, n)	product	yield
(1, 0)		80%	(1, 1)		93%
(2, 1)		89%	(1, 2)		93%

Our results demonstrate that sequential ring-closing metathesis of easily prepared silyloxy ether dienes and subsequent oxidative ring cleavage can be used to prepare a series of *cis*-olefinic polyhydroxy molecules.

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7. Allyl- and vinylchlorodimethysilane was obtained from Aldrich Co. For the preparation of (3-butenyl)chlorodimethylsilane, see: Steinmetz, M.; Yu, C. *J. Org. Chem.* **1992**, *57*, 3107-3120.
8. A representative procedure for RCM of silyloxy dienes: to a solution of diene **9** (400 mg, 1.3 mmol) in CH_2Cl_2 (26 mL, 0.05 M) was added Ru-catalyst **2b** (53 mg, 0.06 mmol, 5 mol%) and the reaction mixture was stirred for 3 h at 25 °C. After evaporation of the solvent, the residue was purified by chromatography on silica gel (EtOAc/hexanes = 1/15) to afford the cyclized product (346 mg, 96%) as a colorless liquid; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.37 (m, 5H), 5.79 (td, *J* = 8.4, 7.8 Hz, 1H), 5.43 (td, *J* = 10.8, 6.0 Hz, 1H), 4.58 (s, 2H), 4.02 (m, 1H), 3.43 (d, *J* = 6.0 Hz, 2H), 2.53 (m, 1H), 2.02 (m, 1H), 1.66 (m, 2H), 1.33 (m, 1H), 0.22 (s, 3H), 0.21 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 138.3, 128.4, 127.5, 127.0, 126.7, 75.5, 73.2, 69.7, 32.8, 22.9, 19.4, -0.6, -2.8.
9. (a) Miller, S. J.; Kim, S.-H.; Chen, Z.-R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2108-2109. (b) Clark, J. S.; Kettle, J. G. *Tetrahedron Lett.* **1997**, *38*, 123-126 and 127-130.
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11. A representative procedure for oxidative cleavage of silyloxy cycloolefeins: to a solution of the cyclized alkene (m = 2, n = 1, Table 2 in the text) (330 mg, 1.2 mmol) in THF/MeOH (5 mL/5 mL) was added KF (346 mg,6.0 mmol) and $KHCO_3$ (284 mg,2.8 mmol) and then followed by a 30%-H_2O_2 solution (1.2 mL, 10.6 mmol). After stirring for 12 h at room temperature, the crude mixture was extracted with EtOAc (30 mL x 2), washed with brine (50 mL), dried over $MgSO_4$, and then evaporated. Chromatography on silica gel (EtOAc/hexanes = 2/1) provided the desired product (248 mg, 89 %) as aliquid; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.43 (m, 5H), 5.67 (td, *J* = 10.8, 6.6 Hz, 1H), 5.52 (td, *J* = 10.8, 8.1 Hz, 1H), 4.54 (s, 2H), 4.20 (dd, *J* = 9.6, 3.6 Hz, 1H), 4.07 (dd, *J* = 12.6, 6.3 Hz, 1H), 3.82 (m, 1H), 3.46 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.55 (dd, *J* = 7.2, 3.6 Hz, 1H), 3.31 (s, 2H), 2.32 (m, 1H), 2.14 (m, 1H), 1.50 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 137.9, 132.3, 129.4, 128.1, 127.9, 128.5, 74.7, 73.4, 69.1, 57.9, 32.5, 23.3.

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