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# Synthesis of Oxygenated Heterocycles From Cyclic Allylsiloxanes Using Ring-Closing Olefin Metathesis

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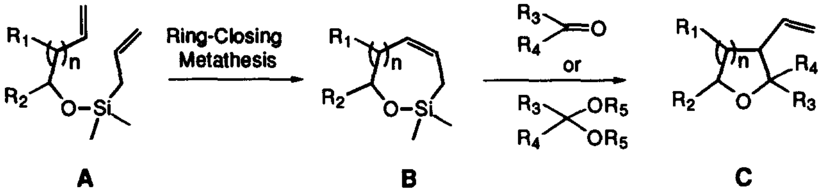
**Abstract:** Cyclic allylsiloxanes were prepared from allyldimethylsilyl ethers of various alkenols by using a catalytic ring-closing metathesis (RCM) reaction. The transformation of these cyclic allylsiloxanes into stereoselectively substituted tetrahydrofurans and tetrahydropyrans was achieved by using a silyl modified Sakurai reaction. © 1997 Elsevier Science Ltd.

Recently, the construction of carbo and heterocycles by catalytic ring-closing olefin metathesis has emerged as a powerful synthetic tool.[1] Transition metal catalyzed processes especially ruthenium-carbene catalysts are particularly selective for the transformation of polyfunctional precursors of enhanced complexity. This methodology is now finding increasing use in synthesis.[2-5]

A recent report from Grubbs et al.[6] prompts us to disclose our own results concerning the construction of cyclic allylsiloxanes of type **B** from allyldimethylsilylethers of type **A** by using a RCM reaction, and their transformation into stereospecifically substituted oxygenated heterocycles **C**.



Allyldimethylsilylethers **1-4** were prepared by silylation of the corresponding alkenols[7] in quantitative yield (method A: AllylMe$_2$SiCl, Et$_3$N, DMAP cat. in CH$_2$Cl$_2$). Alternatively, allyldimethylsilylethers can be obtained by tethering succesively allylmagnesium bromide and alkenols on Et$_2$NSiMe$_2$Cl (method B).[8]

Treatment of a solution of **1-4** in dichloromethane or benzene by a catalytic amount of Cl$_2$(PCy$_3$)$_2$Ru=CHPh[9] (3 to 6 mol%) under the conditions indicated, leads to the formation of the corresponding cyclic allylsiloxanes **5-8** in good to moderate yields (Table 1). We have to point out that compounds with 6-, 7- and 8-membered rings were obtained under similar conditions in good yield. When a substituent was present at C-2 (compound **8**), the ruthenium catalyst was sensitive to steric effects[6] and the yields were somewhat lower.

Since compounds **5-8** contain an allylic silane, the condensation of those compounds with aldehydes, ketones and ketals has been achieved under Sakurai modified conditions.[10] Carbonyl compounds or their ketals were reacted with compounds **6-8** in dichloromethane at -78°C in the presence of a catalytic amount of

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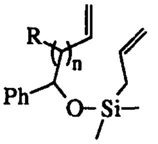
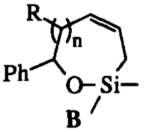
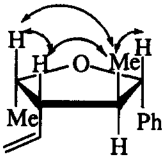
trimethylsilyl triflate (TMSOTf). A smooth reaction ensued, giving the corresponding desired tetrahydrofurans or tetrahydropyrans in good yields and with high diastereoselectivity (Table 2). Examination of the crude material by $^1H$ NMR showed diastereoisomeric ratio (d.r.) up to 95/5.

**Table 1**: Preparation and ring-closing metathesis of allyldimethylsilylethers **A**

| Substrate | Preparation | | Ring-closing olefin metathesis | | | | Products | |
|---|---|---|---|---|---|---|---|---|
|  **A** | Yield(%) [a]<br>Method<br>A | B | Solvent | T | Conc (M) | Time (h) |  **B** | Yield(%) [a] |
| **1** n = 0 , R = H | 99 | 64 | $CH_2Cl_2$ | rt | 0.5 | 1 | **5** | 88 [b] |
| **2** n = 1 , R = H | 99 | 60 | $CH_2Cl_2$ | rt | 0.5 | 3 | **6** | 80 |
| | | | | reflux | 0.5 | 1 | | 88 |
| **3** n = 2 , R = H | 100 | - | $CH_2Cl_2$ | reflux | 0.1 | 3 | **7** | 85 |
| **4** n = 1 , R = Me [c] | 100 | - | $C_6H_6$ | 60°C | 0.1 | 48 | **8** | 31 |
| | | | | 80°C | 0.01 | 48 | | 48 |

a) Isolated yield of analytically pure material after flash column chromatography on silica gel.
b) This sensitive compound was isolated by distillation.
c) *anti* diastereoisomer

The relative configuration of **9**, **10** and **13**[11] have been assigned unambiguously from their $^1H$ NMR spectra with the help of differential nOe experiments (Scheme 1). The relative configurations of **11**, **12**, **14** and **15** have been attributed accordingly .



**Scheme 1**: Observed differential nOe effects in compound **13**

The formation of tetrahydrofurans and tetrahydropyrans can be interpreted in terms of the following hypothetical mechanism. Reaction of the silylether moieties of the cyclic allylsiloxanes with the electrophiles (carbonyl compounds or their acetals activated by the Lewis acid TMSOTf) generates oxonium ions which can be trapped intramolecularly by the allylsilane, thus generating the oxygenated heterocycles and a new Lewis acid species (Scheme 2). A chairlike transition state in which the substituents preferentially occupy pseudo-equatorial positions can account for the stereochemical outcome of this reaction, which parallels the results previously obtained in a related kind of cyclization.[10c]

**Scheme 2**: Mechanism for the formation of tetrahydrofurans and tetrahydropyrans

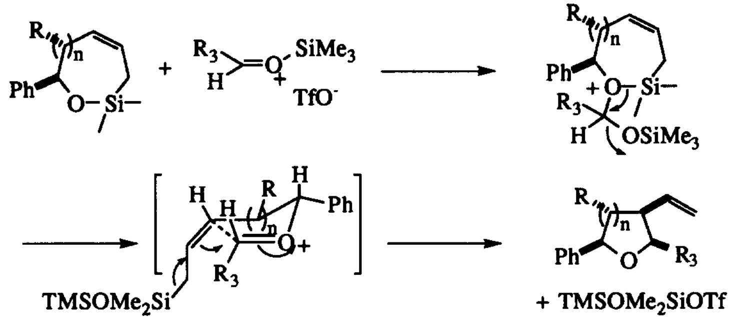
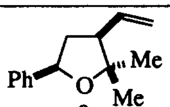
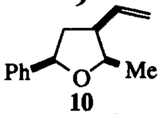
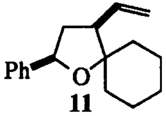
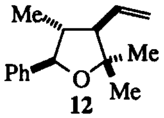
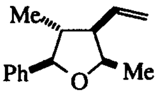
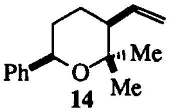
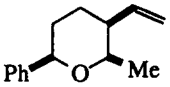


**Table 2**: Transformation of cyclic allylsiloxanes into oxygenated heterocycles

| Substrate | Electrophile [a] | Product | Yield (%) [b] |
|---|---|---|---|
| **6** | Me$_2$C(OMe)$_2$ |  **9** | 82 |
| | MeCHO |  **10** | 83 |
| | Cyclohexanone |  **11** | 70 |
| **8** | Me$_2$C(OMe)$_2$ |  **12** | 72 |
| | MeCHO |  **13** | 78 |
| **7** | Me$_2$C(OMe)$_2$ |  **14** | 85 |
| | MeCHO [c] |  **15** | 84 |

a) A solution of **6-8** and of the electrophile (3 equiv for Me$_2$C(OMe)$_2$, 3 equiv for MeCHO and 1 equiv for cyclohexanone) was treated at -78°C with TMSOTf (10-15 mol%) for 30 min.
b) Isolated yield of analytically pure material after flash column chromatography on silica gel.
c) The reaction mixture was warmed up to -50°C.

We have shown that RCM reactions can be used to build silicon containing heterocycles. The latter compounds subjected to a modified Sakurai reaction can lead to substituted tetrahydrofurans or tetrahydropyrans.

Further work is in progress to apply this methodology in natural product synthesis.

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## References and Notes

1. a- Schmalz, H. G. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1833-1836.
   b- Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426-5427.
   c- Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 7324-7325.
   d- Kim, S.-H.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 10801-10802.
2. Borer, B. C.; Deerenberg, S.; Bieraügel, H.; Pandit, U. K. *Tetrahedron Lett.* **1994**, *55*, 3191-3194.
3. Schuster, M.; Pernerstorfer, J.; Blechert, S. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1979-1980.
4. Yang, Z.; He, Y.; Vourloumis, D.; Vallberg, H.; Nicolaou, K. C. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 166-168.
5. a- Rutjes, F. P. J. T.; Schoemaker, H. E. *Tetrahedron Lett.* **1997**, *58*, 677-680.
   b- Barrett, A. G. M.; Baugh, S. P. D.; Gibson, V. C.; Giles, M. R.; Marshall, E. C.; Procopiov, P. A. *J. Chem. Soc., Chem. Commun.* **1997**, 155-156.
6. Chang, S.; Grubbs, R. H. *Tetrahedron lett.* **1997**, *38*, 4757-4760.
7. a- The alkenols corresponding to **1**, **2**, **3** were respectively prepared by addition of vinyl, allyl and 3-buten-1-yl magnesium bromide to benzaldehyde.
   b- The alkenol corresponding to **4** (*anti* diastereoisomer) was obtained by addition of crotylchromium halide to benzaldehyde: Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179-3181.
8. a- Stork, G.; Keitz, P. F. *Tetrahedron Lett.* **1989**, *30*, 6981-6984.
   b- $Et_2NSiMe_2Cl$ was prepared according to: Tamao, K.; Nakajo, E.; Ito, Y. *Tetrahedron* **1988**, *44*, 3997-4007.
9. Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100-110.
10. a- Mekhalfia, A.; Markó, I. E. *Tetrahedron Lett.* **1991**, *52*, 4779-4781.
    b- Mekhalfia, A.; Markó, I. E., Adams, H. *Tetrahedron Lett.* **1991**, *52*, 4783-4786.
    c- Markó, I. E.; Bayston, D. J. *Tetrahedron Lett.* **1993**, *34*, 6595-6598.
11. **Compound 13**: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$: 7.38-7.27 (5H, m), 5.80-5.67 (ddd, $J$ = 16.6, 10.7, 9.5 Hz, 1H), 5.14-5.07 (2H, m), 4.40-4.33 (2H, m), 2.65-2.56 (1H, m), 1.94-1.79 (1H, m), 1.28 (d,$J$ = 6.6 Hz, 3H), 0.97 (d, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 141.3, 136.5, 128.2, 127.4, 126.2, 116.9, 87.8, 76.9, 55.8, 46.8, 18.6, 13.9; MS *m/z*: 202 ($M^+$, 0.6), 158 (85), 143 (100), 129 (62), 115 (21).

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