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A new access to various functionalised trimethylsilyl substituted carbo- and heterocycles

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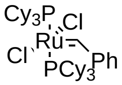
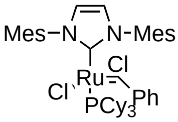
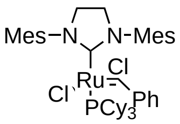
Abstract—Trimethylsilyl substituted carbo- and heterocycles could be efficiently prepared using a ring closing metathesis reaction of the corresponding silylated dienes. © 2002 Elsevier Science Ltd. All rights reserved.

Silyl olefins are widely utilised as versatile synthetic intermediates.[1] The Si–C bonds in alkenylsilylanes are amenable to cleavage in the presence of fluoride, generating carbon nucleophiles that can react further with a variety of electrophiles or alternatively, undergo cross-coupling reactions with vinyl or aryl halides in the presence of palladium catalysts.[2] Silylated olefins can also undergo electrophile-induced substitution reactions in a similar fashion to arylsilanes.[3] In addition, they are direct precursors of epoxysilanes which are also valuable intermediates in organic synthesis since they can undergo regioselective and stereospecific ring opening with a range of nucleophiles to give β-hydroxysilanes or can be hydrolysed to give carbonyl compounds.[4]

Further to our studies on the use of vinylsilanes for electrophilic fluorodesilylation processes,[5] we embarked on the development of a general strategy towards the synthesis of various functionalised trimethysilyl substituted cycloalkenes. Ring closing metathesis catalysed by ruthenium or molybdenum complexes has revolutionised the way in which carbocycles and heterocycles are constructed and therefore, we anticipated that the ring closing metathesis might emerge as a powerful tool for the preparation of diverse functionalised trimethylsilyl olefins.[6] Several groups have recently reported on the metathesis reactions of vinylalkoxysilane derivatives as well as on the cross coupling of cycloalkenylsiloxanes.[2,7] We now report on the preparation and ring closing metathesis of vinyltrimethylsilyl substituted dienes **1a**–**i**. The reactivity of these dienes towards the ruthenium-based ring closing metathesis catalysts **2**,[8] **3**[9] and **4**[10] was examined.



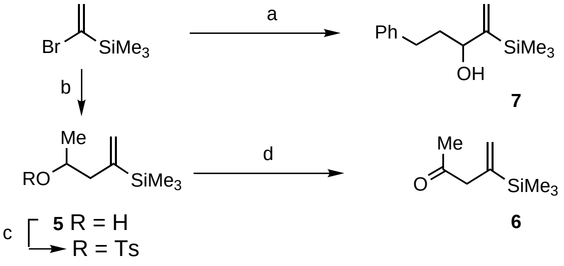




Mes = 2,4,6-trimethylphenyl

2 **3** **4**

The dienes were prepared according to standard procedures (Schemes 1 and 2). *C*-Alkylation of the commercially available diethylallylmalonate afforded diene **1a** in 44% yield.[11] The azadiene **1b** was obtained by reductive amination of ketone **6** with allylamine followed by *N*-protection with an overall yield of 81%.[12] The β,γ-unsaturated ketone **6** was prepared by oxidation of the corresponding secondary alcohol **5**, a product resulting from the ring opening of propylene oxide with 1-lithio-1-trimethylsilylethylene.[13] Dienes **1c**–**i** were all prepared



Scheme 1. Synthesis of compounds **5**–**7**. (a) *t*BuLi, ether, −78°C then $PhCH_2CH_2CHO$, ether, −78°C to rt, 74%; (b) *t*BuLi, ether, −78°C then propylene oxide, ether, −78°C to rt, 73%; (c) TsCl, pyridine, 0°C to rt, 5 h, 84%; (d) $(COCl)_2$, DMSO, Et_3N, DCM, −60°C to rt, 1 h, 86%.

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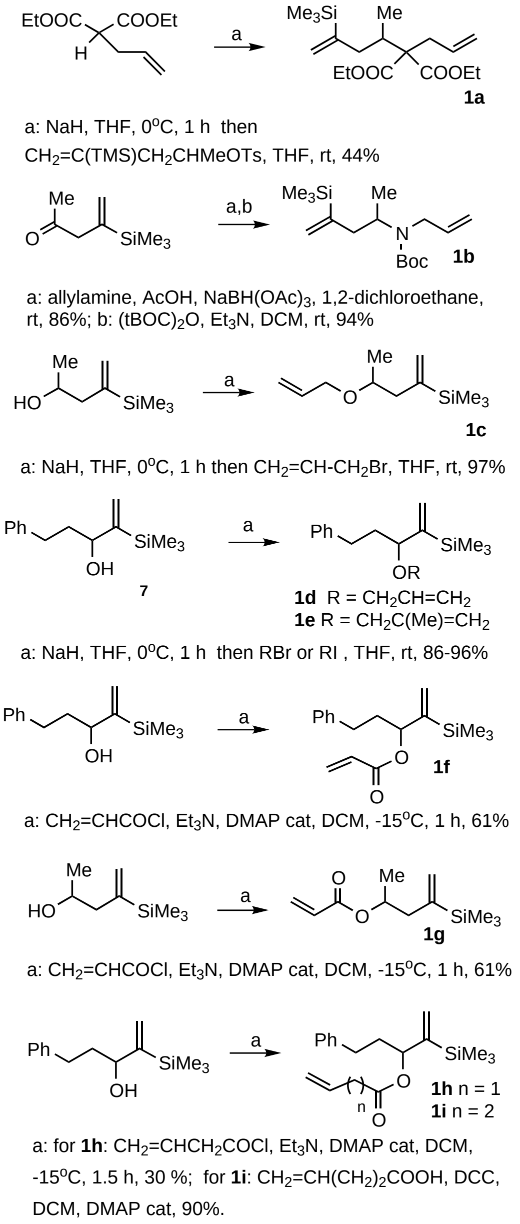
by a Williamson ether synthesis or by acylation starting with alcohols **5** or **7** in chemical yields ranging from 86% to 97%. Alcohol **7** was obtained in 74% yield by addition of 1-lithio-1-trimethylsilylethylene to hydrocinnamaldehyde.[12]

Initially, it was necessary to determine if the ruthenium alkylidenes **2**, **3** and **4** were active for the RCM of dienes containing a trimethylsilyl substituted olefin. Initial attempts to cyclise diene **1c** using the Grubbs' catalyst **2** failed. Analysis of the crude mixture revealed the presence of starting material only and none of the desired product. Even the more reactive catalyst **3** failed to promote the RCM reaction of diene **1c** efficiently. Indeed, only 12% conversion could be obtained after 15 hours in refluxing dichloromethane using 2 mol% of catalyst **3**. Gratifyingly, diene **1c** did undergo the RCM process using the ruthenium complex **4** as the catalyst (entry 3, Table 1). After optimisation, a near quantitative yield of compound **8c** was isolated after 3 hours of reaction in the presence of 3 mol% of **4** in refluxing dichloromethane. No dimerisation product could be detected in the crude mixture. Similarly, the carbocycle **8a** was obtained in almost quantitative yield after 8 hours reaction in the presence of 3 mol% catalyst **4** (entry 1, Table 1). Ring closure of the *N*-Boc protected diene **1b** leading to the corresponding 4-trimethylsilyl-3,6-dehydro-2*H*-pyridine **8b** proved feasible but required an increase in the catalyst load to 5 mol% and extended reaction time in order to achieve high yield (entry 2, Table 1). To further illustrate the potential of this technology, the RCM of some ethers and esters was investigated. Diene **1d** was the most reactive substrate as it underwent cyclisation to afford the five-membered ring **8d** in 90% yield after just 1 h in the presence of 2 mol% catalyst **4** (entry 4, Table 1). Interestingly, catalyst **4** also cyclised substrate **1e** despite the significant increase in steric demand. However, for this reaction, 12 mol% catalyst was used to afford product **8e** in 83% yield after 29 h (entry 5, Table 1). Finally, the methodology allowed the preparation of the five- and six-membered α,β-unsaturated lactones **8f** and **8g** in good yields albeit at the expense of extended reaction times (entries 6 and 7, Table 1). This might be explained by the formation of an unproductive metal chelate as hypothesised previously by Fürstner and Ghosh.[14] Attempts to cyclise dienes **1h–i** were unsuccessful, resulting in the formation of the non-cyclic dimers **8h** and **8i** (entry 8, Table 1). For both dimers, the *E* stereoisomer was the major product.[15] In light of the longevity of the catalyst, the *Z*:*E* ratios could result from subsequent isomerisation of the initial products.



a: NaH, THF, 0°C, 1 h then $CH_2=C(TMS)CH_2CHMeOTs$, THF, rt, 44%

a: allylamine, AcOH, $NaBH(OAc)_3$, 1,2-dichloroethane, rt, 86%; b: $(tBOC)_2O$, Et_3N, DCM, rt, 94%

a: NaH, THF, 0°C, 1 h then $CH_2=CH-CH_2Br$, THF, rt, 97%

a: NaH, THF, 0°C, 1 h then RBr or RI , THF, rt, 86-96%

a: $CH_2=CHCOCl$, Et_3N, DMAP cat, DCM, -15°C, 1 h, 61%

a: $CH_2=CHCOCl$, Et_3N, DMAP cat, DCM, -15°C, 1 h, 61%

a: for **1h**: $CH_2=CHCH_2COCl$, Et_3N, DMAP cat, DCM, -15°C, 1.5 h, 30 %; for **1i**: $CH_2=CH(CH_2)_2COOH$, DCC, DCM, DMAP cat, 90%.

Scheme 2.

Herein, we have presented a brief survey of the behaviour of ruthenium catalysts **2**, **3** and **4** with the silicon-containing substrates **1a–i**. In addition to previous reports on metathesis reactions of silicon containing substrates where the silicon functionality served as a temporary tethering group, our work has demonstrated that the ring closing metathesis could be applied to the preparation of a series of functionalised trimethylsilyl substituted carbo- or heterocycles.[16] These findings further illustrate the high activity and functional group compatibility of the catalyst **4** and significantly expand the number of substrates that can participate in this powerful reaction.

Acknowledgements

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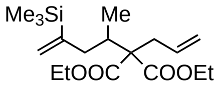
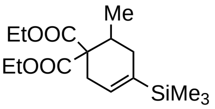
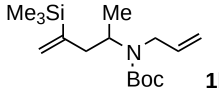
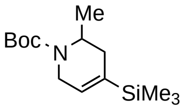
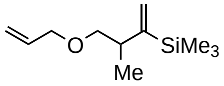
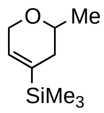
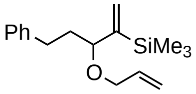
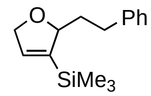
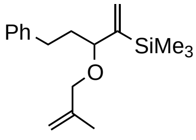
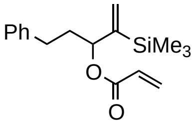
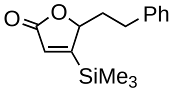
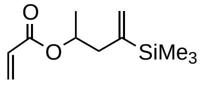
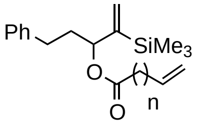
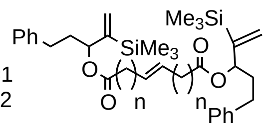
Table 1. Results of the RCM of trimethylsilyl substituted dienes **1a**–**i**

Entry	Substrates	Products	yield[a] mol % of **4** reaction time
1	 **1a**	 **8a**	98% 3 mol % 8 h
2	 **1b**	 **8b**	93% 5 mol % 18 h
3	 **1c**	 **8c**	93% 3 mol % 3 h
4	 **1d**	 **8d**	90% 2 mol % 1 h
5	 **1e**	 **8e**	83% 12 mol % 29 h
6	 **1f**	 **8f**	86% 10 mol % 36 h
7	 **1g**	 **8g**	79% 8 mol % 72 h
8	 **1h** n =1 **1i** n = 2		**8h** n = 1 87% *E*:*Z* = 73:27 4 mol %, 17 h **8i** n = 2 84% *E*:*Z* = 66:34 6 mol %, 25 h

a: isolated yields

References

1. (a) Chen, T. H.; Fleming, I. *Synthesis* **1979**, 761; (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988; (c) *The Chemistry of Organosilicon Compounds*; Patai, S.; Rappoport, Z., Eds; Wiley: Chichester, 1998.
2. (a) Denmark, S. E.; Yang, S.-M. *Org. Lett.* **2001**, *11*, 1749; (b) Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 6439 and references therein.
3. An excellent review on the nucleophile or electrophile induced cleavage of Si–C bonds is presented in: Brook, M. *Silicon in Organic, Organometallic, and Polymer Chemistry*; John Wiley & Sons, 2000; Part III, Chapter 16.
4. Hudrlik, P. F.; Hudrlik, A. M. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI: Greenwich, 1993; Vol. 2, pp. 1–89.
5. Greedy, B.; Gouverneur, V. *Chem. Commun.* **2001**, 233.
6. For recent reviews, see for example: (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012; (b) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413; (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed.* **1997**, *36*, 2036.

7. (a) Pietraszuk, C.; Fisher, H.; Kujawa, M.; Marciniec, B. *Tetrahedron Lett*. **2001**, *42*, 1175; (b) Pietraszuk, C.; Maciniec, B.; Fisher, H. *Organometallics* **2000**, *19*, 913; (c) one example in Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc*. **2000**, *122*, 3783; (d) Feher, F. J.; Soulivong, D.; Eklund, A. G.; Wyndham, K. D. *Chem. Commun*. **1997**, 1185.
8. (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed*. **1995**, *34*, 2039; (b) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc*. **1996**, *118*, 100; (c) Belderrain, T. R.; Grubbs, R. H. *Organometallics* **1997**, *16*, 4001.
9. (a) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc*. **1999**, *121*, 2674; (b) Huang, J.; Schanz, H.-J.; Stevens, E. D.; Nolan, S. P. *Organometallics* **1999**, *18*, 5375; (c) Fürstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem*. **2000**, *65*, 2204.
10. (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett*. **1999**, *1*, 935; (b) Bielawski, C. W.; Grubbs, R. H. *Angew. Chem., Int. Ed*. **2000**, *34*, 1234.
11. Doran, W. J.; Shonle, H. A. *J. Am. Chem. Soc*. **1937**, *59*, 1625.
12. See for example Senboku, H.; Kajizuka, Y.; Hasegawa, H.; Fujita, H.; Suginome, H.; Orito, K.; Tokuda, M. *Tetrahedron* **1999**, *55*, 6465.
13. Martin, L. D.; Stille, J. K. *J. Org. Chem*. **1982**, *47*, 3630.
14. (a) Fürstner, A.; Langermann, K. *J. Am. Chem. Soc*. **1997**, *119*, 9130; (b) catalyst **2** in the presence of a Lewis acid: Ghosh, A. K.; Cappiello, J.; Shin, D. *Tetrahedron Lett*. **1998**, *39*, 4651; (c) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc*. **2000**, *122*, 3783.
15. Z:E ratios based on ^{1}H NMR spectra. The E isomer of product **8h** has been synthesised independently from *trans*-β-hydromuconic acid for unambiguous assignment of the stereochemistry.
16. During the preparation of this manuscript, Marciniec et al. published a paper on the cross-metathesis of vinylsilanes with allyl alkyl ethers catalysed by ruthenium–carbene complexes: Kujawa-Welten, M.; Pietraszuk, C.; Marciniec, B. *Organometallics* **2002**, *21*, 840.