An Intramolecular Diels–Alder Reaction of Vinylsilanes

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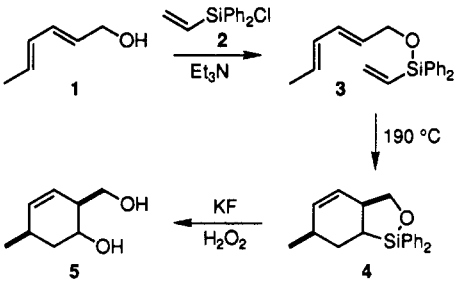
Summary: Dialkylvinylsilyl ethers of dienols undergo a smooth intramolecular Diels–Alder reaction to yield a versatile bicyclic product with an endo–exo selectivity influenced by the substituents on silicon.

The "temporary silicon connection" pioneered by Stork[1a] has proven a valuable synthetic artifice, based in part on the versatility of the silicon–carbon bond.[2] Studies in this area have highlighted the silyl ether as a tether component for reactions such as radical cyclization[1] and hydrosilylation.[3] Recently, several groups have described a variation of this theme: an intramolecular Diels–Alder (DA) reaction[4] in which silicon unifies a diene and a dienophile through an unsymmetrical silyl diether or where silicon anchors the tether to the diene.[5] We report here the use of vinylsilanes as dienophiles in an intramolecular DA reaction.[6] *Inter*molecular DA reactions with vinylsilane dienophiles have received modest attention,[7] primarily as acetylene equivalents.

We envisioned that dialkylvinylsilyl halides, readily prepared by hydrosilylation[8] or organometallic coupling, would easily form an ether with a dienyl alcohol and the resulting triene could then be thermally cyclized. The presence of a silicon–oxygen bond would be advantageous, as the carbon–silicon bonds in the product could be directly transformed into a carbon–carbon bond[9] or a carbon–oxygen bond[10] with retention of stereochemistry.

Scheme I



The efficacy of the reaction sequence was demonstrated using the commercially available sorbyl alcohol 1 and diphenylvinylchlorosilane 2. Triene ether 3 was taken up in toluene and warmed to 190 °C overnight. This served to fully convert 3 to the heterobicycle 4 as a 1:1 mixture of isomers (NMR). Unfortunately, isolation by silica gel chromatography was plagued by an apparently reversible hydrolysis of one of the isomers. Isolation was therefore postponed until after Tamao oxidation[11] and diol 5[12] was isolated as a 1:1 mixture of isomers.

The steps in Scheme I can be consolidated into a single operation. Such a sequence avoids unnecessary manipulations and allows the use of dimethylvinylsilyl ethers that would be too moisture sensitive for silica gel chromatography. In a typical protocol, a mixture of alcohol 1 and excess triethylamine in toluene was treated with a slight excess of dimethylvinylchlorosilane. The resulting mixture was filtered into a resealable tube and heated to 190 °C overnight. Upon cooling and addition of methyllithium, trimethylsilyl-substituted alcohols 8 and 9 were isolated in 68% overall yield (Table I, entry 2).

Additional examples of this reaction sequence are shown in Table I. Notably, tether lengths of three or four atoms (Table I, entries 1–4) proceed with equal efficiency. A five-atom tether (entry 5), however, is converted only slowly to a DA product, presumably for entropic reasons, and substantial amounts of triene remained after the thermolysis. Two different workup procedures, Tamao oxidation to give a diol or addition of methyllithium to give a trimethylsilyl-substituted alcohol, produce equivalent yields of product.

Comparison of reactions that employ the dimethylsilyl group with those using the diphenylsilyl group, particularly entries 1, 2, 6, and 7, indicated that the alkyl substituent on silicon influences the endo–exo selectivity. Stereogenic control by a temporary, sterically-adjustable group such as silicon would provide significant versatility in a synthetic

(1) For lead references see: (a) Stork, G.; Kim, G. *J. Am. Chem. Soc.* **1992**, *114*, 1087. (b) Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *56*, 3085. (c) Myers, A. G.; Gin, D. Y.; Widdowson, K. L. *J. Am. Chem. Soc.* **1991**, *113*, 9661.

(2) Colvin, E. W. In *The Chemistry of the Metal–Carbon Bond*; Hartley, F. R., Ed.; John Wiley & Sons: New York, 1987; Vol. 4, Chapter 6, pp 539–621.

(3) For lead references see: Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1992**, *57*, 1643. Anwar, S.; Bradley, G.; Davis, A. P. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1383. Tamao, K.; Tohma, T.; Inui, N.; Nakayama, O.; Ito, Y. *Tetrahedron Lett.* **1990**, *31*, 7333.

(4) For reviews of the intramolecular Diels–Alder reaction see: Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon: New York, 1990. Roush, W. R. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI: Greenwich, CT, 1990; Vol. 2, pp 91–146 and references cited therein.

(5) (a) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478. (b) Shea, K. J.; Zandi, K. S.; Staab, A. J.; Carr, R. *Tetrahedron Lett.* **1990**, *31*, 5885. (c) Craig, D.; Reader, J. C. *Tetrahedron Lett.* **1990**, *31*, 6585. (d) Gillard, J. W.; Fortin, R.; Grimm, E. L.; Maillard, M.; Tjepkema, M.; Bernstein, M. A.; Glaser, R. *Tetrahedron Lett.* **1991**, *32*, 1145. (e) Shea, K. J.; Staab, A. J.; Zandi, K. S. *Tetrahedron Lett.* **1991**, *32*, 2715.

(6) Wilson has reported an example of an intramolecular DA reaction of a β-trimethylsilyl acrylamide: Wilson, S. R.; Di Grandi, M. J. *J. Org. Chem.* **1991**, *56*, 4766.

(7) For examples see: Wagner, G. H.; Bailey, D. L.; Pines, A. N.; Dunham, M. L.; McIntire, D. B. *Ind. Eng. Chem.* **1953**, *45*, 367. Goodman, L.; Silverstein, R. M.; Gould, C. W. *J. Org. Chem.* **1957**, *22*, 596. Ponomarenko, V. A.; Snegova, A. D. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1960**, 135. Kuivila, H. G.; Warner, C. R. *J. Org. Chem.* **1964**, *29*, 2845. Cunico, R. F. *J. Org. Chem.* **1971**, *36*, 929. Cunico, R. F.; Dexheimer, E. M. *Organomet. Chem. Synth.* **1971**, *1*, 253. Fleming, I.; Patel, S. K. *Tetrahedron Lett.* **1981**, *22*, 2321. Paquette, L. A.; Williams, R. V. *Tetrahedron Lett.* **1981**, *22*, 4643. Tamao, K.; Yoshida, J.-i.; Yamamoto, H.; Kakui, T.; Matsumoto, H.; Takahashi, M.; Kurita, A.; Murata, M.; Kumada, M. *Organometallics* **1982**, *1*, 355. Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *J. Org. Chem.* **1984**, *49*, 3235. Carr, R. V. C.; Williams, R. V.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 4976. Hermeling, D.; Schäfer, H. J. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 233. Ebeling, S.; Matthies, D.; McCarthy, D. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1991**, *60*, 265. Singleton, D. A.; Martinez, J. P. *Tetrahedron Lett.* **1991**, *32*, 7365.

(8) Ojima, I, In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: New York, 1989; Vol. 2, Chapter 25. Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 8, Chapter 3.12.

(9) Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Tetrahedron* **1992**, *48*, 2113. Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1990**, *31*, 2719. Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Heterocycles* **1990**, *30*, 303.

(10) Colvin, E. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 7, Chapter 4.3.

(11) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694.

(12) All new compounds were characterized by ^1H and ^{13}C NMR, IR, MS, and combustion analysis or HRMS.

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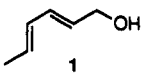
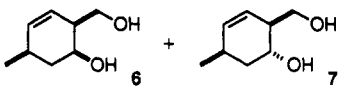
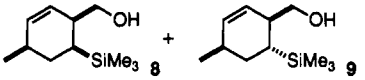
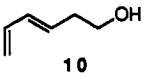
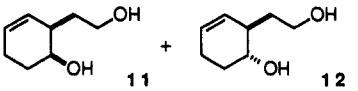
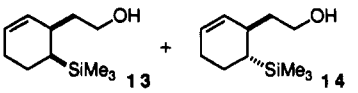
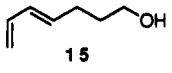
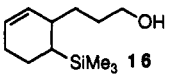
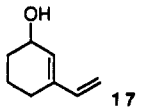
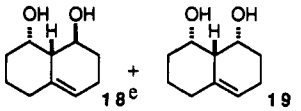
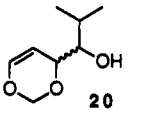
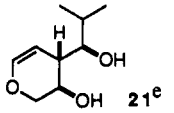
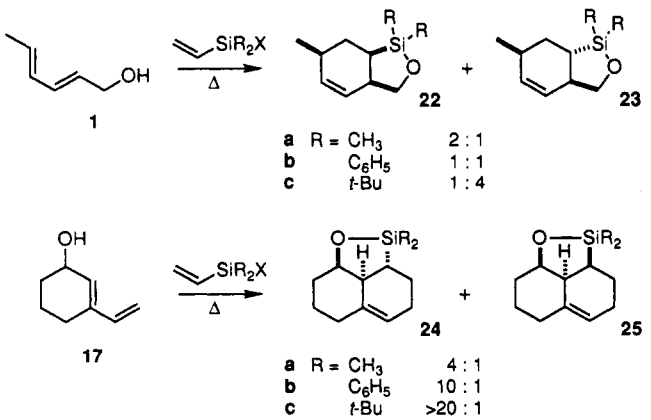
Table I

entry	dienol	$C_2H_3R_2SiCl$	condns[a]	products	yield[b] (%)	ratio[c]
1	 1	R = Ph	A	 6 + 7	71	1:1
2	1	R = CH_3	B	 8 + 9	68	2:1
3	 10	R = Ph	A	 11 + 12	75	1:1
4	10	R = CH_3	B	 13 + 14	72	1:1
5	 15	R = CH_3	B	 16	25	nd
6	 17	R = CH_3	A	 18[e] + 19	64	4:1
7	17	R = Ph	A	18 + 19	73[d]	10:1
8	 20	R = CH_3	A	 21[e]	40	f
9	20[g]	R = Ph	A	21	75[d]	f

[a] A: a solution of the silyl ether in toluene, formed by mixing the dienol and chlorosilane with triethylamine and DMAP (cat.) in toluene and filtering, was heated to 190 °C for 20 h, cooled, concentrated in vacuo, and then treated with KF, $KHCO_3$, and 30% hydrogen peroxide in a mixture of methanol and THF (1:1) at ambient temperature (R = Me) or reflux (R = Ph). B: a solution of silyl ether in toluene, formed by mixing the dienol and chlorosilane with triethylamine and DMAP (cat.) in toluene and filtering, was heated to 190 °C for 20 h, cooled, and then treated with excess methyllithium at ambient temperature. [b] Yields of chromatographically isolated material, >95% pure, based on the amount of starting dienol. [c] Ratios determined by GC or NMR and/or isolation of each isomer. [d] Yields based on isolated triene silyl ether. [e] Structure determined by X-ray.[22] [f] Only one isomer observed. [g] A 1:1 mixture of diastereomers.

Scheme II



sequence. To probe this point, the known di-*tert*-butylvinylfluorosilane[13] was prepared. Although we were initially unsure of our ability to cleanly substitute fluorine for oxygen, in view of the relative strengths of their bonds to silicon,[14] this proved to be facile and the di-*tert*-butylvinyl silyl ethers of 1 and 17[15] were readily prepared. A tabulation of the endo–exo selectivity for the three vinylsilanes with alcohols 1 and 17 is shown in Scheme II. With sorbyl alcohol 1, a dimethylsilyl group yields a 2:1 ratio of products in which the major isomer results from an endo approach of the silicon. This result is consistent with the observation that the steric influence of methyl silanes is small,[16] an effect attributable to the length of the silicon–carbon bond relative to a carbon–carbon bond.[17] Changing to a diphenylsilyl group yields a 1:1 ratio of

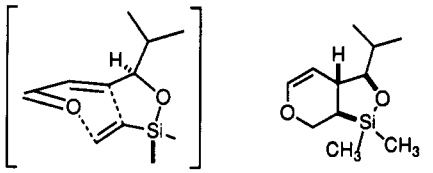
(13) Auner, N. *Z. Anorg. Allg. Chem.* **1988**, *558*, 87.

(14) Walsh, R. *Acc. Chem. Res.* **1981**, *14*, 246.

(15) For intramolecular Diels–Alder reactions of dienes related to 17, see: Funk, R. L.; Mossman, C. J.; Seller, W. E. *Tetrahedron Lett.* **1984**, *25*, 1655. Hecker, S. J.; Heathcock, C. H. *J. Org. Chem.* **1985**, *50*, 5159.

(16) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618. Kitching, W.; Olszowy, H. A.; Drew, G. M.; Adcock, W. *J. Org. Chem.* **1982**, *47*, 5153.

(17) For a review of the steric influence of the trimethylsilyl group, see: Hwu, J. R.; Wang, N. *Chem. Rev.* **1989**, *89*, 1599.



26

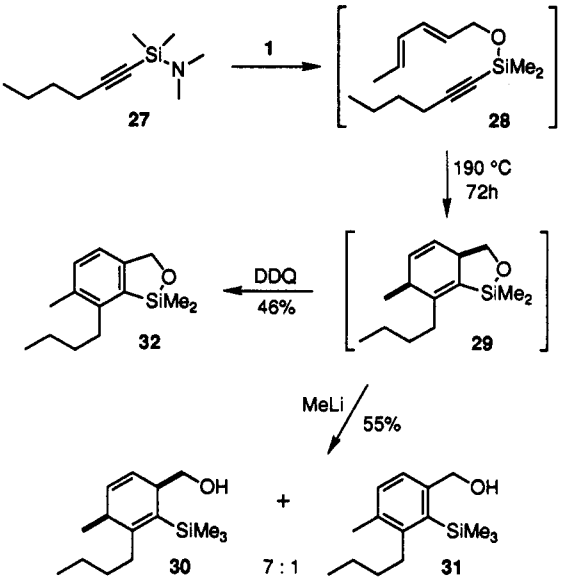
Figure 1.

products, and the di-*tert*-butylsilyl group results in largely the exo-derived product with an isomer ratio of 1:4.[18] In contrast, cycloaddition of the dimethylvinylsilyl ether of dienol **17** yields a predominantly exo product, and increasing the size of the silicon substituent progressively increases the selectivity of the cycloaddition. Changing methyl to phenyl changes the ratio of isomers from 1:4 to 1:10, while a di-*tert*-butylsilyl group results in the formation of a single isomer.[19]

Entries 8 and 9 illustrate the use of a heterodiene[20] and the effect of a stereogenic center. Dioxene alcohol **20**, prepared by the method of Funk,[21] was subjected to our standard conditions with both dimethyl and diphenylvinylsilanes. In both cases the expected retro-DA-DA-Tamao oxidation sequence proceeded smoothly and only a single isomer could be detected for compound **26** or the final product **21**. The relative configurations were confirmed by X-ray crystallography.[22] This isomer presumably results from a transition state that minimizes nonbonding interactions (Figure 1).

Initial evaluation of alkynyl silanes[23] as dienophiles in this reaction sequence has found these to be similarly useful. The rate of cycloaddition for **28** is slower than for the vinylsilanes, requiring 72 h at 190 °C for complete reaction. The cyclohexadiene product **29** (Scheme III) is also more labile, suffering significantly from aromatization under the reaction conditions. Addition of BHT (5 mol %) to the solution largely eliminates this problem. Thermolysis followed by treatment with methyllithium yields cyclohexadiene **30** (55%), contaminated with 15% of the aromatized **31**. Compound **31** is not observed in the

Scheme III



crude reaction mixture but appears to have formed during isolation. Treatment of the crude thermolysis product with DDQ serves to aromatize cyclohexadiene **29**, and **32** is isolated in 46% yield. The heterocyclic ring of **32** is surprisingly stable to chromatography, in view of our experience with **4**, and does not suffer from hydrolysis of the silyl ether during silica gel chromatography.

We have demonstrated the efficiency of an intramolecular Diels–Alder reaction of vinylsilyl ethers for assemble of uniquely functionalized intermediates. Several key features of the reaction have been elucidated, including the effect of tether length, the control of stereogenesis by alkyl substituents on silicon, as well as by a stereogenic center on the tether. Alkynyl silyl ethers appear to be similarly useful.

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Supplementary Material Available: Detailed experimental procedures for the preparation of **6–9** and physical data for compounds **6–9, 11–14, 16, 18, 19, 21,** and **30–32** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) The assignment of cis and trans ring fusion is based on the expected effect of steric interactions and a striking resemblance of the NMR spectra of cycloaddition products **4** with the DA products derived from allyl 2,4-hexadienyl ether. We thank Dr. Kenneth J. O'Connor for providing copies of these spectra: O'Connor, K. J. Ph.D. Thesis, University of Rochester, 1989.

(19) Compounds **22c, 23c, 24c** and **25c** have proven resistant to oxidation of the silicon–carbon bond. The effect of the steric environment on the oxidation of silicon–carbon bonds is currently under investigation.

(20) For examples see: Martin, S. F.; Benage, B.; Geraci, L. S.; Hunter, J. E.; Mortimore, M. *J. Am. Chem. Soc.* **1991**, *113*, 6161 and references cited therein. For a review of the thermal cycloaddition chemistry of unsaturated carbonyl compounds see: Desimoni, G.; Tacconi, G. *Chem. Rev.* **1975**, *75*, 651.

(21) Funk, R. L.; Bolton, G. L. *J. Am. Chem. Soc.* **1988**, *110*, 1290.

(22) The authors have deposited atomic coordinates for compounds **18** and **21** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(23) Prepared by the method of Stork and Keitz: Stork, G.; Keitz, P. F. *Tetrahedron Lett.* **1989**, *30*, 6981.

Addition of Germylenes to α,β-Unsaturated Acetals: A Net [2,3] Sigmatropic Rearrangement

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Summary: Addition of germanium dichloride dioxane complex to α,β-unsaturated acetals gives β-dichloroalkoxygermane enol ethers via a net [2,3]-sigmatropic rearrangement.

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