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Diastereoselectivity in Cyclopropanation and Epoxidation Reactions of Chiral (*E*)-Crotylsilanes: Asymmetric Synthesis of Substituted Tetrahydrofurans

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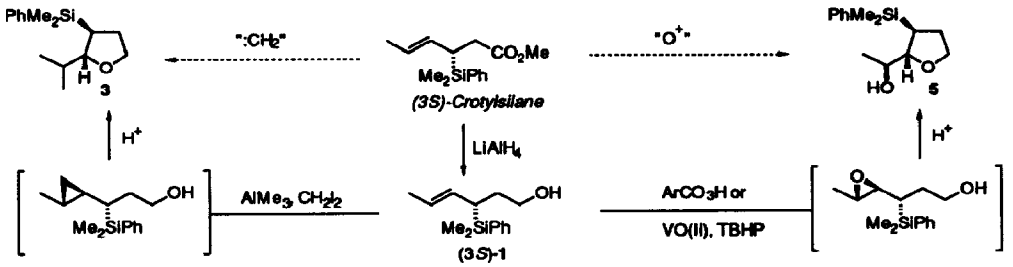
Abstract. Functionalized (*E*)-crotylsilanes **1** bearing a bis-homoallylic hydroxyl group undergo diastereoselective cyclopropanation and epoxidation reactions to produce substituted tetrahydrofurans **3** and **5** respectively after an acid catalyzed heterocyclization.

Research conducted in our laboratories has established the utility of chiral (*E*)-crotylsilanes as reagents for highly diastereo- and enantioselective condensation reactions with acetals.[1] In subsequent reports we have described enantioselective tetrahydrofuran annulations based on Lewis acid promoted addition reactions of the silane reagents to achiral and chiral aldehydes.[2] Those studies resulted in the development of a useful strategy for the asymmetric construction of 2,5-cis and 2,5-trans substituted tetrahydrofurans and documented the participation of chiral (*E*)-crotylsilanes in a highly diastereoselective tetrahydrofuran annulation. The historical importance of cyclopropanes and epoxides in organic synthesis has helped provide the stimulus to further probe the utility of our developing chiral allylsilane bond construction methodology. We have learned that the crotylsilanes **1**, bearing a primary hydroxyl group derived from a $LiAlH_4$ reduction of the corresponding ester undergo cyclopropanation and epoxidation reactions with useful levels of diastereoselection. The two processes result in the formation of silyl-functionalized tetrahydrofurans. This study expands the scope of these silane reagents in acyclic stereocontrol and illustrates how: (i) the stereocenter bearing the silicon group directs the addition to one of the π-faces of the adjacent olefin and the stereoselective heterocyclization, (ii) the σ-donating silicon group activates the cyclopropyl and epoxide rings by $\sigma \rightarrow \sigma^*$ orbital overlap, stabilizing the emerging β-carbocation. The two electrophilic substitution processes are illustrated in Scheme I leading to their respective silyl-functionalized furans.

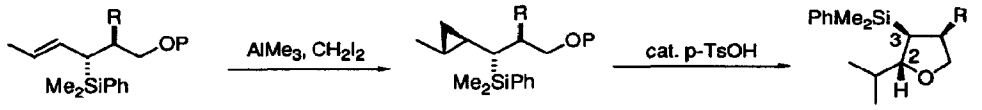
Scheme I



Previous studies have demonstrated that chiral allyl-,[3] vinyl-[4] allenylsilanes,[5] as well as secondary allylic alcohols[6] participate in stereoselective cyclopropanation and epoxidation reactions. Based on those reports we projected that chiral (*E*)-crotylsilane reagents would show useful levels of selectivity in similar electrophilic additions. In this Letter, we wish to report the results of our experiments concerning the $AlMe_3$-CH_2I_2 promoted cyclopropanation. We are also disclosing comparative results of peracid and VO(II)-TBHP catalyzed epoxidations of the illustrated chiral silane reagents. Representative examples obtained for the electrophilic addition processes with the silane reagents are summarized in Tables I and II.[7]

Tetrahydrofurans via Diastereoselective Cyclopropanations of *(E)*-Crotylsilanes. The tetrahydrofurans **3**, were produced in nearly diastereomerically pure form under mild reaction conditions (entries 1-3, Table I).[8] In a two-step sequence: [i] a diastereoselective cyclopropanation employing a modified Simmons-Smith[9] reaction with the known aluminum complex $AlMe_3$-CH_2I_2,[10] followed by; [ii] treatment of the mixture of cyclopropanes **2**, with a catalytic amount of *p*-TsOH (CH_2Cl_2, RT) afforded the tetrahydrofurans in high yield. The substituted alcohols **1b** and **1c** showed greater selectivity in the cyclopropanation while the presence of the hydroxy group on the reagent increased the rate of reaction as well as the selectivity, compare entries 1 and 4 in Table I. Interestingly, the parent methyl ester (Scheme I) reacted only very slowly, and exhibited no selectivity under the cyclopropanation conditions described above.

Table I



1 2 3

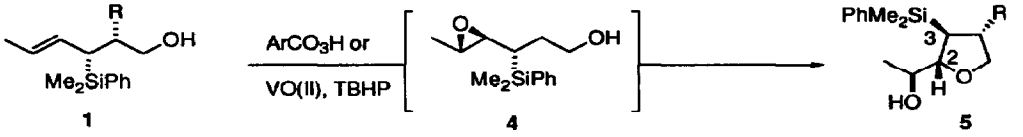
Entry	Crotylsilane	Diastereoselectivity [anti / syn] (%yield **2**)[a]	Tetrahydrofuran Product **3** % yield	(2,3-anti : syn)[b]
1.	(3*S*)-**1a**, R = P = H	3 : 1 (79 %)	86%	> 30 : 1
2.	(2*R*, 3*S*)-**1b**, R = Me, P = H	20 : 1 (81 %)	74%	> 30 : 1
3.	(2*R*, 3*S*)-**1c**, R = Bn, P = H	6 : 1 (67 %)	79%	> 30 : 1
4.	(3*S*)-**1d**, R = H, P = ^{t}BuPh$_2$Si	1.5 : 1 (67 %)	------	------

[a] All $AlMe_3$ promoted cyclopropanations were run in CH_2Cl_2, with CH_2I_2 (2.8 equiv) at 0 °C and allowed to warm to ambient temperature for 8 h. [b]Assignment of relative stereochemistry was based on difference N.O.E. measurements. Absolute stereochemistry is assigned by analogy based on the chirality of starting crotylsilane.

Tetrahydrofurans via Diastereoselective Epoxidations of *(E)*-Crotylsilanes. In an analogous manner, the crotylsilane bis-homoallylic alcohols undergo highly diastereoselective

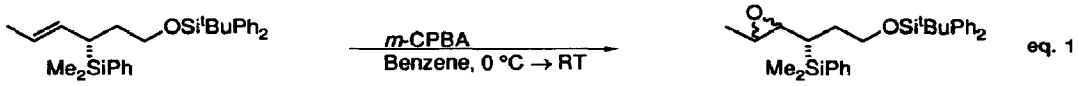
epoxidation reactions promoted by *m*-CPBA[11] or VO(acac)$_2$-TBHP.[12] In the examples shown below in Table II, the hydroxyl group helps to support the sense of diastereoselection by working synergystically with the topology of the trans-olefin substrate.[13] In general, high levels of selectivity were observed both for peracid and transition metal-catalyzed epoxidation/cyclization as the furans were isolated directly from the reaction mixture. The sensitivity of the reaction diastereoselection to the presence of the hydroxyl group is shown below in equation 1. In contrast to the examples in Table II, when the primary alcohol is protected the *m*-CPBA-catalyzed epoxidation proceeded without selectivity.[14]

Table II



entry	Crotylsilane	Epoxidation conditions[a, b]	Tetrahydrofuran Product 5 % yield	(2,3-anti : syn)[c]
1.	(3*S*)-**1a**, R = H	*m*-CPBA (1.5 equiv)	**5a** 81%	(6 : 1)
2.	(3*S*)-**1a**, R = H	VO(acac)2 (0.05 equiv) / TBHP (2 equiv)	**5a** 68%	(15 : 1)
3.	(2*R*, 3*R*)-**1d**, R = OMe	*m*-CPBA (1.5 equiv)	**5b** 66%	(19 : 1)
4.	(2*R*, 3*R*)-**1d**, R = OMe	VO(acac)2 (0.05 equiv) / TBHP (2 equiv)	**5b** 54%	(15 : 1)
5.	(2*R*, 3*S*)-**1e**, R = Bn	*m*-CPBA (1.5 equiv)	**5c** 70%	(30 : 1)
6.	(2*R*, 3*S*)-**1e**, R = Bn	VO(acac)2 (0.05 equiv) / TBHP (2 equiv)	**5c** 46%	(15 :1)
7.	(2*S*, 3*R*)-**1f**, R = Me	*m*-CPBA (1.5 equiv)	**5d** 50%	(15 : 1)
8.	(2*S*, 3*R*)-**1f**, R = Me	VO(acac)2 (0.05 equiv) / TBHP (2 equiv)	**5d** 20%	(20 : 1)

[a] All reactions utilizing meta-chloro perbenzoic acid were run in dry benzene (18 h). [b] The reactions that used catalytic VO(acac)$_2$ and TBHP were run in CH_2Cl_2 for 3 h at 0 °C and then 12 h at room temperature. [c] Assignment of relative stereochemistry was based on difference N.O.E. measurements. Absolute stereochemistry is assigned by analogy based on the chirality of starting crotylsilane.



eq. 1

Diastereoselection = 1 : 1

The isolation of the 2,3-anti isomer is consistent with the stepwise mechanism proposed to rationalize the formation of related tetrahydrofurans; initial electrophilic addition occurs by an anti addition[15] followed by the formation of a stabilized β-silyl carbocation. The intrinsic stereoselectivity of the fundamental S_N2-like process predicts that the hydroxyl group will trap the emerging carbocation with inversion of the original stereochemistry at the C2 position.

In conclusion, the use of chiral (*E*)-crotylsilanes in cyclopropanation and epoxidation reactions provides a highly stereoselective process for the formation of silyl-functionalized tetrahydrofurans and continues to expand the scope and utility of this emerging allyl metal chemistry.

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References and Notes

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1 (a) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868-9870. (b) Panek, J. S.; Yang, M. *J. Org. Chem.* **1991**, *56*, 5755-5758. (c) Panek, J. S.; Yang, M; Xu, F. *J. Org. Chem.* **1992**, *57*, 5790-5792.

2 (a) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868-9870. (b) Panek, J. S.; Beresis, R. T. *J. Org. Chem.* **1993**, *58*, 809-811.

3 Fleming, I.; Sarkar, A. K.; Thomas, A. P. *J. Chem. Soc., Chem. Commun.*, **1987**, 157-158.

4 Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1992**, *58*, 798-800.

5 Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1993**, *58*, 5037-5039.

6 Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1987**, *52*, 3944-3946.

7 All new compounds were isolated as chromatographically pure materials and exhibited ^{1}H NMR, ^{13}C NMR, IR, MS, and HRMS spectral data consistent with their assigned structure.

8 (a) Traditional Simmons/Smith cyclopropanation [Zn/Cu, CH_2I_2 (3.0 equiv), cat. I_2, in refluxing Et_2O for 4 h] and the samarium metal promoted reactions were conducted [CH_2I_2 in THF from -78 °C → RT]. However, both failed to produce detectable amounts of product.

9 (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323-5324. (b) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256-4264.

10 Maruoka, K.; Fukutani, Y.; Yamamoto, H. *J. Org. Chem.* **1985**, *50*, 4414-4415.

11 Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1973**, 1958-1965.

12 Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136-6137.

13 For an excellent and comprehensive review concerning substrate-directable reactions see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307-1370.

14 Related epoxidations see: Murphy, P. J.; Russell, A. T.; Procter, G. *Tetrahedron Lett.* **1990**, *31*, 1055-1058.

15 (a) Fleming, I. in *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon Press Oxford, 1991; vol. 2. pp 563-593. For a discussion concerning the mechanisms and stereochemistry of S_E'-type reactions see: (b) Matassa, V. G.; Jenkins, P. R.; Kumin, A.; Damm, L.; Schreiber, J.; Felix, D.; Zass, E.; Eschenmoser, A. *Israel J. Chem.* **1989**, *29*, 321-343. (c) Panek, J. S. *Comprehensive Organic Synthesis*, Schreiber, S. L., Ed.; Pergamon Press: Oxford, **1991**, Vol 1, 596-593.

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