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CHELATION CONTROLLED ALLYLATION OF ALDEHYDES WITH A CHIRAL ALLYLSILYLENE DERIVED FROM (–)-10-PHENYLPINANEDIOL

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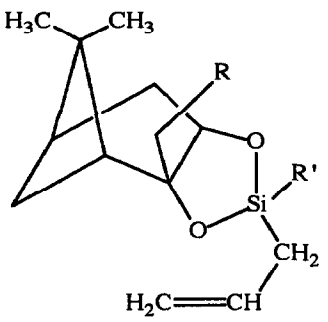
Abstract: The chiral allylsilylene prepared from (–)-10-phenylpinanediol reacts with chiral α-alkoxy aldehydes in the presence of stannic chloride to afford homoallylic alcohols with diastereofacial selectivity ratios as high as 100:0. The results are consistent with attack of the allylsilylene on the less hindered face of the chelated intermediate. Our preliminary studies on several silylenes prepared from bicyclo[3.1.1] systems revealed that substituent effects on the chiral auxiliary and the silicon atom play an important role in the selectivity of these unique compounds.

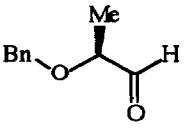
In recent years, allyl- and crotylmetallation of the carbonyl group have been developed as versatile and powerful synthetic routes to homoallylic alcohols.[3] Furthermore, these processes have proven amenable to the exertion of high degrees of both absolute and relative stereochemical control. Allyl- and crotyl boronates, titanates and stannanes have been the subjects of the most intense scrutiny. The organosilicon equivalent, the Hosomi-Sakurai reaction, has also been utilized in asymmetric versions for stereoselective carbon-carbon bond formation.[4] Simple achiral allylsilanes have been shown to add in an anti-Cram manner to α- and β-alkoxysubstituted aldehydes under conditions of chelation control. Typical syn/anti ratios of > 90:10 have been reported for these single stereodifferentiating processes. Studies by Reetz support a non-cyclic, synclinal addition mechanism which parallels the Masamune aldol reaction.[5] In reactions of chiral silicon reagents with achiral carbonyl compounds, good to excellent enantiomeric excesses have been obtained where a stereogenic carbon is incorporated in an allylic position adjacent to the metal atom. However, results in reactions where the stereogenic center resides at silicon or at remote sites in a chiral auxiliary have been much less promising.[6]

On the other hand, very little attention has been directed to the topic of double stereodifferentiation in the Hosomi-Sakurai reaction even though it appears as though very high levels of stereoselection may be attainable by this approach. A single example of this methodology has demonstrated excellent diastereoselectivity from self-selection of reaction partners in the condensation of a racemic allylsilane (stereocenter at α-carbon) and a racemic, non-chelating aldehyde.[7]

Herein, we detail some preliminary results of a study directed at developing a synthetically useful double stereodifferentiating version of the Lewis acid-catalyzed allylation of aldehydes which employs chiral silylenes endowed with homochiral centers both at silicon and at more remote sites in pinanediol-derived auxiliaries.



Allylsilylene



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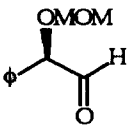

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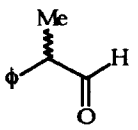

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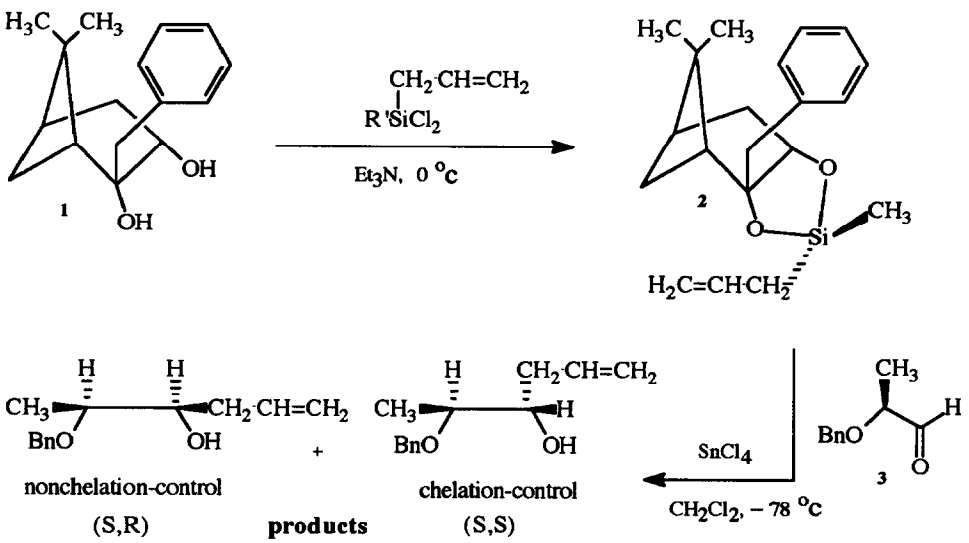
During the initial phase of our studies we chose to examine both (+)- and (–)-pinanediol as chiral auxiliaries, since each was commercially available and had been successfully used by Matteson et.al.[8] for the preparation of chiral boronate esters. At the same time, it was possible to probe possible steric effects of phenyl and methyl substitutents on the silicon atom by making silylenes derived from allylphenyl- and allylmethyldichlorosilane. Finally, the influence of Lewis acid catalysis was investigated since several groups[9] have reported distinct stereoselective differences for titanium tetrachloride and stannic chloride mediated reactions. The chiral aldehydes used in our study included two compounds capable of **intra**molecular chelation, (S)-2-(benzyloxy)propanal **3** and (R)-methoxymethoxyphenylethanal **4**, and another, (dl)-2-phenylpropanal **5**, which coordinates only in an **inter**molecular fashion. In summary, we found that silylenes derived from (–)-pinanediol and allylmethyldichlorosilane (R'=Me, R=H) afforded diastereomeric ratios of 89:11 to 80:20 while the corresponding silylenes derived from allylphenyldichlorosilane (R'=Ph, R=H) were much less selective having ratios of 73:27 to 55:45. The chemical yields of homoallylic alcohols from these reactions ranged from 87-46%. Overall, the more effective chelating ability of stannic chloride afforded higher yields and more predictable stereochemical results than did titanium tetrachloride mediated reactions. Finally, the versatile nature of the silylene platform was demonstrated by its ability to control facial selectivity during these reactions by exchange of the (–)-pinanediol auxiliary for its antipode, (+)-pinanediol. For example, the silylene derived from allylmethyldichlorosilane and (–)-pinanediol gave predominantly **si**-facial selectivity whereas the corresponding silylene from allylmethyldichorosilane and (+)-pinanediol displayed **re**-facial selectivity with (S)-2-(benzyloxy)propanal in the presence of stannic chloride. See Table for comparison of the allylsilylenes.

Encouraged by these results, we chose to examine the allyl transfer properties of a chiral allylsilylene **2** produced from (–)-10-phenylpinanediol **1**. This system utilizes a silicon atom not only as a chiral center from which the allyl group is transferred, but also as a unit of a chiral auxiliary platform. Furthermore, the silylene-oxygen atoms provide ligand sites which can coordinate with the Lewis acid catalyst and, thereby, help direct the stereochemistry of the reaction. Finally, steric contributions to this process were maximized by use of the phenyl group at the 10-position of the chiral platform. This group shields the top face of the silylene and forces reaction to occur from the bottom of the molecule. From a practical standpoint, the chiral bicyclic diol platform of the silylene is fully recyclable and, thus, eliminates the need to replenish the chiral auxiliary for subsequent reactions.

Scheme



The silylene **2** required for this study was prepared by reaction of the pinanediol[10] **1** with allylmethyldichlorosilane (R'=Me) in a methylene chloride solution containing triethylamine at 0 °C. A stable[11] silylene was isolated in 50% chemical yield as a single diastereomer having the S-configuration at silicon.[12] Silylene **2** smoothly effected allylation of aldehydes **3,4,5** in the presence of stannic chloride at –78 °C in a methylene chloride solution[13] with chemical yields of 72-55%. The reaction with aldehyde **3** furnished a 100:0 diastereomeric mixture of the (S,S):(S,R)-isomers in accord with chelation-control for asymmetric induction.[14] Likewise, aldehyde **4** afforded a 92:8 diastereomeric mixture. However, when internal chelation with a Lewis acid catalyst was not possible, as in the case of aldehyde **5**, very little stereoselectivity was observed as evidenced by a 59:41 diastereomeric product mixture.

TABLE

Reactions of Chiral Allylsilylenes and Chiral Aldehydes

Pinane	R	R'	Aldehyde	Product Ratio*	Yield,%
(–)	Ph	Me	3	100:0	72
			4	92:8	68
			5	59:41	55
(–)	H	Me	3	80:20	83
			4	85:15	49
			5	89:11	58
(+)	H	Me	3	27:73	87
			4	15:85	50
			5	88:12	54
(–)	H	Ph	3	55:45	32
			4	67:33	67
			5	73:27	46

*Chelation:Non-chelation or Cram:anti-Cram (aldehyde 5)

References and Notes

1. (a) Taken, in part, from a thesis by K. Shanmuganathan in partial fulfillment of the requirements for the Ph.D. degree in organic chemistry, University of Maine, Orono, ME 04469.
   (b) A preliminary account of this work was presented at the 199th National Meeting, ACS, Boston, MA, April, 1990.
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11. Previous reports describe silylenes as being very unstable to Lewis acids, water, and chromatographic materials, see:
   (a) Trost, B. M.; Caldwell, C. G. *Tetrahedron Lett.* **1981**, *22*, 4999.
   (b) Corey, E. J.; Hopkins, P. B. *Tetrahedron Lett.* **1982**, *23*, 4871.
12. 2D-NOSEY NMR showed 9-15% enhancement between the Si-methyl and phenyl group but no enhancement between the allyl and phenyl groups. In comparison, (+)- and (–)-pinanediol allylsilylenes were 59:41 diastereomeric S:R-mixtures.
13. **Typical Procedure:** Stannic chloride (0.16 g, 0.60 mmol, 0.6 mL of 1M solution in methylene chloride) was added to a solution of aldehyde **3** (0.10 g, 0.60 mmol) in dry methylene chloride (3 mL) cooled in a dry ice/acetone bath while stirring and under an atmosphere of dry nitrogen gas. To the stirred mixture was added (–)-10-phenylpinanediol allyl-methylsilylene **2** (0.24 g, 0.74 mmol) dissolved in methylene chloride (3 mL). Stirring was continued for 2-3 h at low temperature. The reaction was quenched with water and extracted into methylene chloride. The combined extracts were washed with water and dried over anhydrous magnesium sulfate. The (S,S)-diastereomer (0.090 g, 72%) was obtained as the sole product. Its proton-NMR was identical with the one provided to us by Professor Clayton Heathcock (Ref. **9a**).
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