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Synthesis of Optically Active Secondary Allylic Alcohols from Allylsilanes via Successive Asymmetric Dihydroxylation (AD) and Peterson Olefination Reactions

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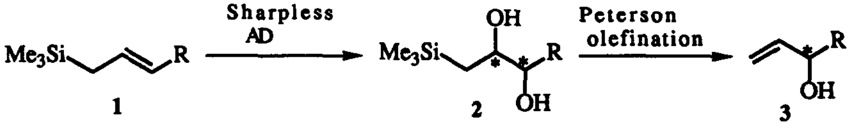
Abstract: *Optically active, secondary allylic alcohols can be prepared from allylic silanes by the successive asymmetric dihydroxylation and Peterson olefination reactions. The Effects of trialkylsilyl groups on the outcome of the AD reaction on vinyl and allyl silanes are also discussed.*

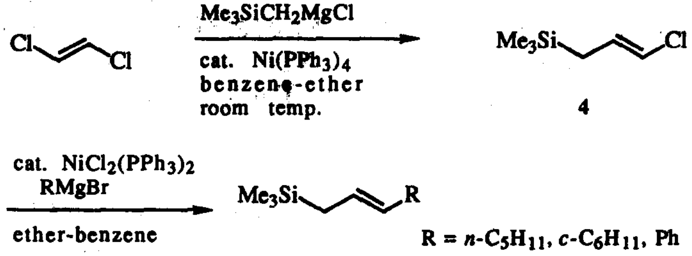
The development of new synthetic routes to enantiomerically pure allylic alcohols has been the subject of intensive research in recent years.1) Herein we report a two step approach to optically active secondary allylic alcohols. This process utilizes the Sharpless AD reaction2) to catalytically convert allylic silanes to optically active diols; the diols are then treated with potassium hydride in THF (Peterson olefination) to provide allylic alcohols in 46-98% chemical yields and with enantiopurities of 13-96% (Scheme 1, Table 1).3)

Scheme 1



The starting allyl silanes4) were prepared by a new two-step method, as outlined in Scheme 2. The coupling reaction of commercially available (*E*)-1,2-dichloroethylene with Me_3SiCH_2MgCl (prepared from Me_3SiCH_2Cl and Mg) in the presence of a catalytic amount of $Ni(PPh_3)_4$ (1 mol%, prepared *in situ* from $NiCl_2(PPh_3)_2$, PPh_3, and EtMgBr) in ether-benzene (5/1, v/v) furnishes the mono coupling product **4** as a benzene solution of 1.5-2.2 M in 62-79% yield.5,6) Treatment of this benzene solution with Grignard reagents in the presence of $NiCl_2(PPh_3)_2$[7] affords allyl silanes in excellent yields (R = *n*-C_5H_{11} (83 %), R = Ph (91 %), R = *c*-C_6H_{11} (93 %)).

Scheme 2



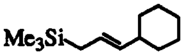
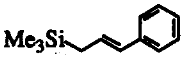
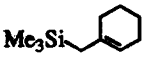
The AD reactions of allylic silanes were investigated with three derivatives of the dihydroquinidine (DHQD) and dihydroquinine (DHQ) class of ligands with the aim of optimizing the enantioselectivity of these reactions. The pair of ligands $(DHQD)_2$-PHAL and $(DHQ)_2$-PHAL, which are considered as the best general ligands for asymmetric dihydroxylation of a variety of olefins,[2] produced a wide range of results with the allylic silanes studied. For instance, with the disubstituted olefins **1a-c** the ee's obtained range from 62 to 96% (entries 5-8). In contrast, however, the trisubstituted olefin **1d** was dihydroxylated with uncharacteristically low enantioselectivity (entries 9 and 10). In accord with the previously well documented propensity of aromatic olefins for yielding high ee's in the AD reaction, the highest ee among these substrates is achieved for the one bearing a phenyl group (**1c**, entry 8). The ligand DHQD-CLB produced better ee's with substrates **1b** and **1d** (entries 2 and 4), but the best overall results were obtained with the ligands DHQD-PHN and DHQ-PHN (entries 12-16).

We have also begun evaluating the effects of trialkylsilyl groups on the outcome of the AD reaction with various ligands on vinyl and allyl silanes (results not in table). Our preliminary results can be summarized as follows. With $(DHQD)_2$-PHAL as the ligand, *vinyl* silanes bearing bulky terminal silyl substituents give low enantioselectivities in the AD reaction. For example, vinyl trimethylsilane is dihydroxylated (AD-mix-β, r.t.) with 46% ee. Interestingly, the presence of the same silyl group in an *allylic* position results in even lower selectivity: allyl trimethylsilane gave the corresponding 1,2-diol with only 13% ee. Finally, the presence of the bulkier silyl group Si(*i*-Pr)$_3$ results in almost no selectivity at all: allyl tri(isopropyl)silane underwent dihydroxylation with 2% ee!

Higher enantioselectivities were obtained with the ligand DHQD-PHN for both vinyl and allyl trimethylsilane: 55% ee and 76% ee, respectively. It is interesting that DHQD-PHN provides higher selectivities with allylic than with vinylic silanes, whereas the opposite trend was observed with $(DHQD)_2$-PHAL.

In conclusion, we have shown that optically active, secondary allylic alcohols can be prepared from allylic silanes by the successive asymmetric dihydroxylation and Peterson olefination reactions. High overall enantioselectivities are obtained by using the ligands DHQD-PHN and DHQ-PHN in the AD reaction.

Table 1

entry	substrate	ligand[a]	2	3[d]	
			yield(%)[b]	confign[c]	optical purity(%ee)[e]
1	 **1a**	DHQD-CLB[f]	93	R	71
2	 **1b**		77	R	82
3	 **1c**		95	S	94
4	 **1d**		–	R	48 (54% yield)[g]
5	**1a**	(DHQD)$_2$-PHAL[i]	76	R	65
6[h]	**1a**		71	R	72
7	**1b**		nd[j]	R	62
8	**1c**		98	S	96
9	**1d**		55	R	15
10[h]	**1d**		nd[j]	R	13
11[h]	**1a**	(DHQ)$_2$-PHAL	77	S	66
12	**1a**	DHQD-PHN[k]	63	R	91
13	**1b**		46	R	95
14	**1c**		87	S	94
15	**1d**		57	R	35
16	**1a**	DHQ-PHN[k]	75	S	87

[a]Structures of chiral ligands; see ref 12. [b] Isolated yield. The AD reactions were carried out at room temperature. [c] The absolute configurations were determined by comparison of the optical rotations with literature values for **3a**[8)], **3c**[9)], **3d**[10)] or that of authentic **3b** prepared from (S,E)-1-Iodo-3-cyclohexyl-prop-1-en-3-ol[11)] via lithiation followed by hydrolysis. [d] To a THF suspension of KH (5mmol) was added diol **2** (1mmol) at -78 °C. This suspension was warmed up to room temperature over 3h and stirred for 1 h. Yields were 77~85%. [e] Enantiomeric excesses were determined by 300 MHz ^{1}H NMR and/or HPLC analysis of the corresponding MTPA esters. [f] 25 mol% ligand was used. [g] Overall yield via 2 steps. [h] 10 mol% ligand was used, however, the optical purity was not improved particularly. [i] AD-mix-β (1 mol% ligand, 0.2 mol% $K_2OsO_2(OH)_4$)[2b)] was used. [j] Not determined. [k] 13 mol% ligand was used.

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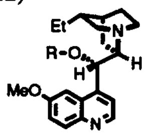
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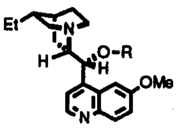
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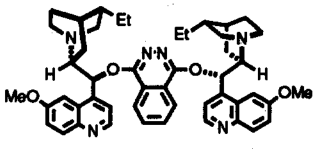
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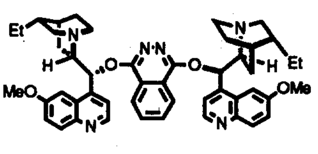
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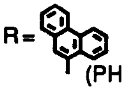
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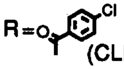
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