

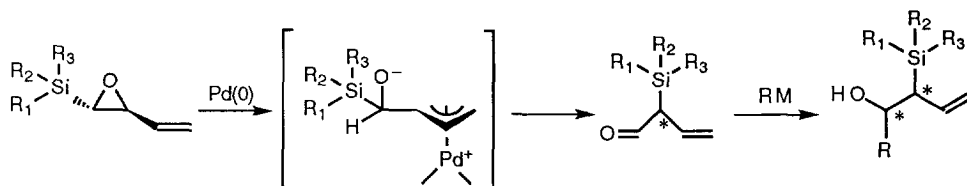
## Total Chirality Transfer in Palladium(0)-Catalyzed Rearrangement of Silicon Substituted Vinyloxiranes

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**Abstract :** The palladium(0)-catalyzed rearrangement of silylated vinyloxiranes occurs with a total transfer of chirality. The absolute stereochemistry of the aldehyde has been determined.

In earlier work, on the palladium(0)-catalyzed rearrangement of silicon substituted vinyloxiranes leading to versatile aldehydes,<sup>1</sup> our attention focused on the generality of this 1,2-silyl migration and on the reactivity of these aldehydes with nucleophiles (Scheme 1).<sup>2</sup>



Scheme 1

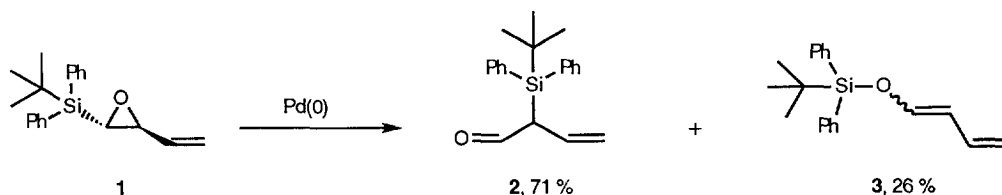
We showed that (i) depending on the size of the silyl substituents, the Brook rearrangement<sup>3</sup> could be competitive, (ii) very interestingly, the addition of organolithium or Grignard reagents on racemic aldehydes furnished the corresponding alcohols with a high level of diastereoselectivity (*de* = 54-98 %).

In order to use such reactions in asymmetric synthesis, mechanistic insight into this novel rearrangement and the assessment of the exact degree of chirality transfer were required. In the literature, very efficient chirality transfers have been achieved in palladium(0)-promoted intra- and intermolecular allylation reactions.<sup>4</sup> In the present work, we report our results concerning the complete chirality transfer in this rearrangement.

For synthetic purposes, we performed the reaction with the *tert*-butyldiphenylsilyl vinyloxirane **1** because this silyl group is easily transformable into hydroxyl group by a Fleming oxidation<sup>5</sup> and in addition, the presence of *tert*-butyl group could impede, in a large extent, the Brook rearrangement.<sup>2</sup>

The vinyloxirane **1** was prepared from commercially available propargyl alcohol.<sup>1</sup> Chirality was introduced *via* an enantioselective Sharpless epoxidation.<sup>6</sup> The enantiomeric excess of **1** was found to be 85 % ee by NMR analysis using the chiral shift reagent (tris[3-heptafluoropropyl-hydroxymethylene]-d-camphorato)europium (III) [Eu(hfc)<sub>3</sub>].

The reaction of **1** with a catalytic amount of palladium(0), generated *in situ* from 1.3 mol % Pd(OAc)<sub>2</sub> and 5.2 mol % P(O*i*Pr)<sub>3</sub>, in tetrahydrofuran at room temperature afforded the aldehyde **2** and the silyldienoether **3** in 71 % and 26 % yields respectively (Scheme 2).

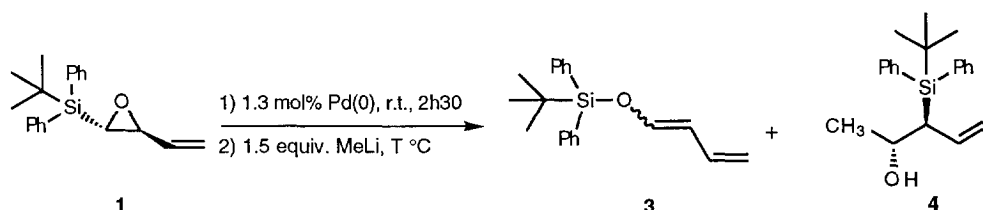


**Scheme 2**

Compared to the *tert*-butyldimethylsilylvinyloxirane which furnished exclusively the corresponding aldehyde **2**, the Brook rearrangement has not been totally avoided in this case because the *tert*-butyl group on silicon did not overcome the electronic effects of the two phenyl groups.<sup>3</sup>

Following the same procedure as reported,<sup>2</sup> we performed in a one-pot sequence both 1,2-silyl migration and addition of the nucleophile. Thus, vinyloxirane **1** was treated, at room temperature, with a catalytic amount of Pd(0), generated as above, followed by 1.5 equivalents of methyllithium at low temperature. The results are presented in the table below.

**Table :** Pd(0)-catalyzed rearrangement of **1** followed by the addition of MeLi



| T(°C) <sup>a</sup> | <b>3</b> (%) | <b>4</b> (%) | <b>4</b> [ $\alpha$ ] <sub>D</sub> <sup>20</sup><br>(c, solvent) | ee (%) |
|--------------------|--------------|--------------|--|--------|
| -78                | 27           | 49           | 30.6 (17, CHCl <sub>3</sub> )                                    | 55     |
| -100               | 28           | 55           | 48.8 (18, CHCl <sub>3</sub> )                                    | 85     |

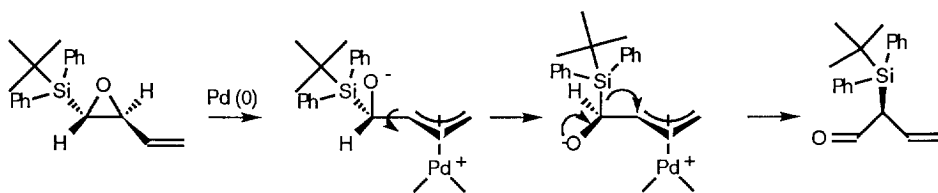
(a) Temperature of the cooling bath.

We showed that the temperature has a dramatic influence on the enantiomeric excess (ee). Indeed, at -78°C the ee of the compound **4**, after its transformation to Mosher esters<sup>7</sup> was typically 55 %, suggesting a partial racemization of the intermediate aldehyde, which is quite sensitive to enolization. To insure a complete transfer of chirality, it was necessary to carry out the reaction at -100°C : the ee was found to be essentially identical, within experimental error, with that of the starting vinyloxirane. Besides, we noticed that when aldehyde **2** is

separated from **3** by flash chromatography before adding the nucleophile, the ee fell to 15 % confirming the easiness of racemization of the aldehyde **2**, even on silica.

After isolation by column chromatography, the absolute configuration of the major diastereomer of Mosher esters of **4** has been determined to be 2R, 3S by the X-ray crystal structure analysis.<sup>8</sup>

On the basis of the complete chirality transfer observed and the diastereoselective addition of the nucleophile which results from the preferred addition of the nucleophile *anti* to the silicon group, according to the Felkin model,<sup>9</sup> we proposed the following mechanistic pathway for the Pd(0)-catalyzed rearrangement of vinyloxiranes (Scheme 3).



Scheme 3

The  $\pi$ -allylpalladium complex was formed by oxidative addition of the vinyloxirane to palladium(0) with inversion.<sup>10</sup> The steric interaction between the silicon and the palladium would favor the rotation around the carbon-carbon bond and furthermore the silylated group would attack *anti* to the metal. The stereochemistry, net retention resulting from double inversion is unambiguously confirmed by the X-ray crystallography data of the resulting Mosher ester derived from **4**.

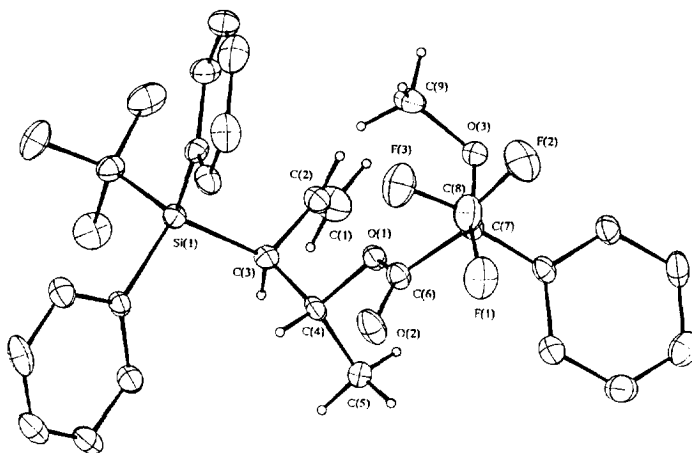
This present study demonstrates that the chiral integrity is preserved in the Pd(0)-catalyzed rearrangement of silylated vinyloxiranes. This new asymmetric preparation of such an ambident precursor, in view of the total diastereoselective addition of nucleophiles, the known stereoselective oxidation of the C-Si bond and the easy stereoselective functionalization of the double bond offer us a new route to prepare enantiomerically pure carbohydrates. This work is under active investigation in our laboratory.

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 (6) We modified the previously described<sup>1</sup> conditions for the enantioselective epoxidation. In this case, the catalytic Sharpless epoxidation was used : 17 % [(+)-DIPT ; Ti(OiPr)<sub>4</sub>], 2 equiv. *t*BuOOH, -25°C, 14 h ; 84 % yield ; 1 [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -20.2 (13, CHCl<sub>3</sub>)  
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 (8) (R)-Mosher acid configuration was used ; the crystal structure of the major Mosher ester of **4** is (on the ORTEP representation C(4) is 2(R) and C(3) is 3(S) :



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