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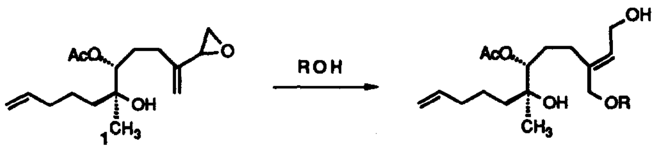
TRIPHENYLSILANOL AS A WATER SURROGATE FOR REGIOSELECTIVE PD CATALYZED ALLYLATIONS

Barry M. Trost, Nobuhiko Ito and Paul D. Greenspan
Department of Chemistry
Stanford University
Stanford, California 94305-5080

Summary: Pd catalyzed reactions of vinyl epoxides and triphenylsilanol provide regioselective introduction of an oxygen nucleophile to create a 2-en-1,4-diol either as a monosilyl ether or a free diol.

Oxygen nucleophiles have proven to be somewhat capricious in Pd(0) catalyzed allylic alkylations.[1-12] Generally, the more stabilized the oxygen nucleophile (eg. carboxylate better than alkoxide) the better partner it is with a π-allylpalladium cation. Water and hydroxide do not show nucleophilic properties towards these intermediates.[13] In cases wherein vinyl epoxides are the substrates, an additional issue arises, regioselectivity.[6,14] In conjunction with a project directed toward the total synthesis of zoapatanol,[15] we confronted the regioselective 1,4-opening of vinyl epoxide **1** (eq. 1). All attempts to effect this reaction using carboxylic acids as the oxygen nucleophile led to high yields of 1:1 adducts but with the 1,2 rather than desired 1,4-products dominating. Attempts to adjust regioselectivity by adding protonic solvents like alcohol or water failed to alter the results significantly. In this paper, we wish to report the development of a new class of oxygen nucleophiles that resolves this problem and permits the equivalent of a nucleophilic addition of water in a one step sequence.



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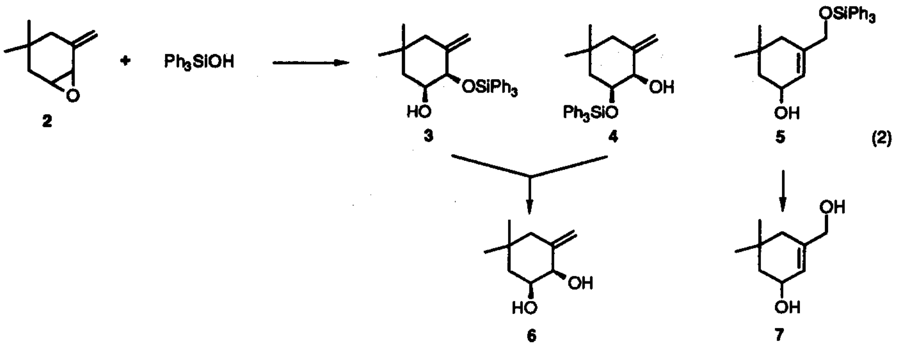
In designing an oxygen nucleophile for regioselective 1,4- addition with vinyl epoxides, we were cognizant that, in contrast to carbon nucleophiles which intrinsically prefer to form the 1,4-regioisomeric product, oxygen nucleophiles intrinsically prefer 1,2-regioselectivity, presumably because of their ability to coordinate by hydrogen bonding to the departing epoxide oxygen and thereby be delivered to the proximal allylic carbon to give the 1,2-adduct. Using a sterically hindered oxygen nucleophile might decrease this coordination and therefore return the regioselectivity to the electronically preferred 1,4- mode; however, a good oxygen nucleophile must be relatively stabilized. Thus, a simple tertiary alcohol does not suffice. Note that attempts to utilize the tertiary alcohol of substrate **1** to achieve cyclization failed whereas an analogous primary alcohol cyclizes without any problems.[16] A silanol appeared to have the correct steric and electronic properties.

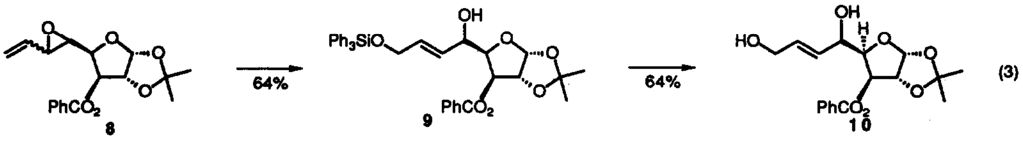
We were pleased to observe that triphenylsilanol reacted smoothly with vinyl epoxide **2** in the presence of a Pd complex [5% $(dba)_3Pd_2 \cdot CHCl_3$, 40% $(iC_3H_7O)_3P$, THF, rt], but it underwent only 1,2-addition to give a regioisomeric mixture of **3**[17] and **4**[18] in 39% and 32% yields respectively with none of the 1,4-adduct **5**. That the two products differed only in the point of attachment of the triphenylsilyl group is easily established by



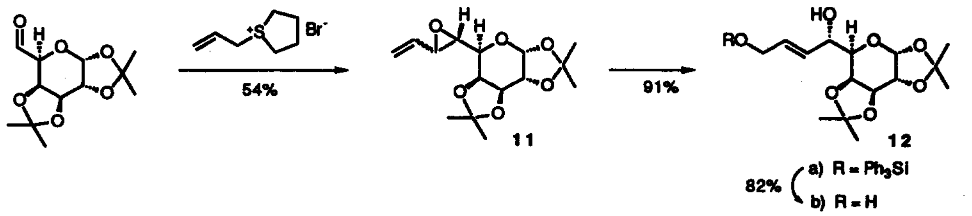
desilylation (KF, CH_3CN, H_2O, 70°) to a single diol **6** whose stereochemistry as *cis* is verified by the 3.3 Hz coupling between the carbinol ring protons.

Changing ligands had no effect on this regioselectivity. Assessing hydrogen bonding between the silanol and the departing epoxide oxygen as the source of the 1,2 regioselectivity as observed for other nucleophiles, we believed the steric hindrance of the silanol might allow exogeneous protonic solvents like water or alcohols to compete favorably for hydrogen bonding but not as nucleophiles. Surprisingly, water proved disappointing, giving only **3** and **4** in the presence of 3 eq. of water and no change in regioselectivity but dramatically reduced yields in the presence of 45 eq. of water. On the other hand, using 4:1 isopropanol:THF with the original catalyst system (vide supra), a 47% yield of the 1,4 product **5** was obtained in addition to 15% and 17% yields respectively of the proximal products **3** and **4**. Use of sterically less demanding bidentate ligands like dppe, dppp and dppb decreased the yields of the proximal products and gave 58-64% yields of the distal product **5**.[17] For optimal rates of reaction, we prefer a catalyst derived from 2% $(dba)_3Pd_2{\bullet}CHCl_3$, 4 mol% dppb and 8 mol% Ph_3P.

Efficacy of trapping by the triphenylsilanol was dependent upon concentration - best results were obtained by running the reactions at least 0.5 M in substrate and 0.78 M in triphenylsilanol. Thus a 70% yield of distal product **5** was obtained. Desilylation as above (88% yield) provided the 1,4-diol **7**[17] quite cleanly. Thus, both proximal and distal diols **6** and **7** are accessible from the same reactants. Using the above as a standard set of conditions, vinyl epoxide **8** was converted into the monosilyl ether of the 1,4-diol **9**[17] (eq. 3) as well as the corresponding diol **10**.[17]

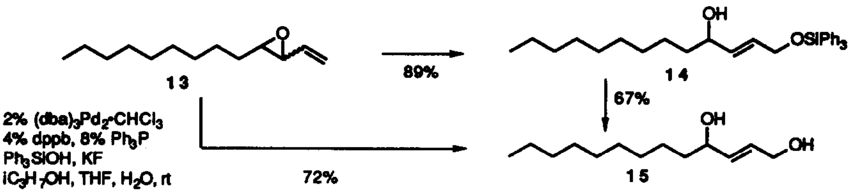


Stereocontrolled construction of side chains onto carbohydrates that may be useful for construction of polyethers combines the diastereoselective nucleophilic epoxidation to epoxide **11** (dr 27:1) with the Pd catalyzed addition of triphenylsilanol to give **12a**[17] (eq. 4). While the vinyl epoxide **11** is an E:Z mixture, the resulting olefin product **12a** possesses only the E geometry. This control of olefin geometry does not require the steric



(4)

bulk of the carbohydrate. The very simple vinyl epoxide **13**, a 3:2 E:Z mixture, also gave only the E-olefinic product **14**[17] which was desilylated (KF, CH_3CN, H_2O) to the 1,4-diol **15**[17] (eq. 5). Since water does not serve as a nucleophile in Pd(0) catalyzed reactions, we explored the one step conversion of the vinyl epoxide **13** to the diol **15**. While effective trapping by triphenylsilanol required maintenance of its concentration at 0.5 M, an effective direct formation of the diol **15** occurred at room temperature wherein the silanol does serve as a catalyst since it remains unchanged after completion of reaction.



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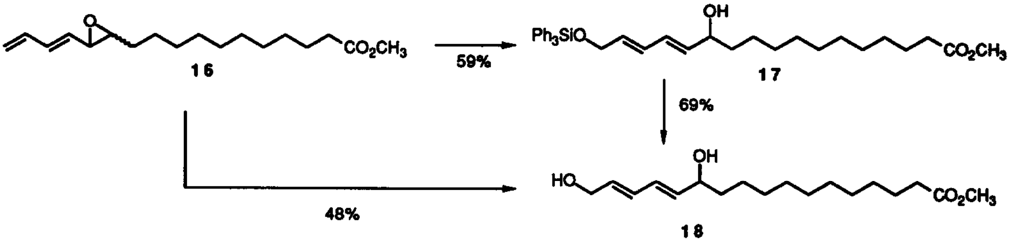
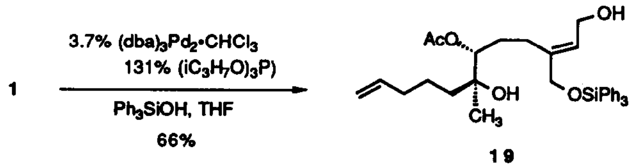
The regioselectivity with a polyene epoxide **16** was also examined. Attack occurred only at the terminal position to give a 9:1 ratio of the E,E:Z,E diene 1,6-diol monosilyl ether **17**[17] and the corresponding diol **18**[17] after standard desilylation. Alternatively, the one step protocol of eq. 5 provided the 1,6-diol directly.



(6)

This method proved effective for the conversion of the vinyl epoxide **1** to the desired 1,4-diol mono-silyl ether (eq. 7) Surprisingly, only the 1,4-product **19**[17] was obtained even using triisopropyl phosphite as ligand in the absence of a protonic solvent! The product possessed only the E-olefin geometry as required for zoapatanol.



(7)

Thus, triphenylsilanol serves as an excellent nucleophile in Pd catalyzed allylic alkylations in which both 1,2 and 1,4 regioisomers may be selectively produced. The convenience of the silyl ether protecting group imparts particular synthetic appeal to this method. Furthermore, the ability to achieve a direct one step conversion of the vinyl epoxides to 1,4-diols illustrates the use of triphenylsilanol as a water surrogate.

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