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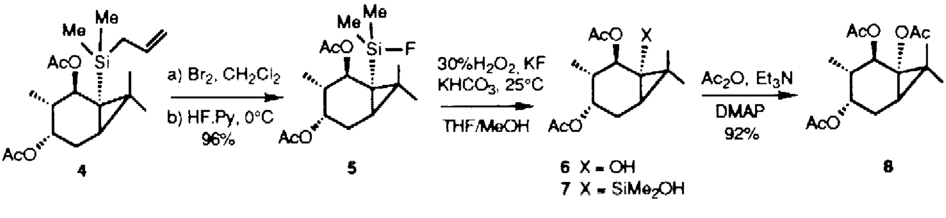
Synthesis of Tertiary Alcohols via the Use of the Allyldimethylsilyl Moiety as a Latent Hydroxyl Group in the Kumada-Fleming-Tamao Reaction.

Sharad S. Magar and P. L. Fuchs*
Department of Chemistry, Purdue University, West Lafayette, IN 47907

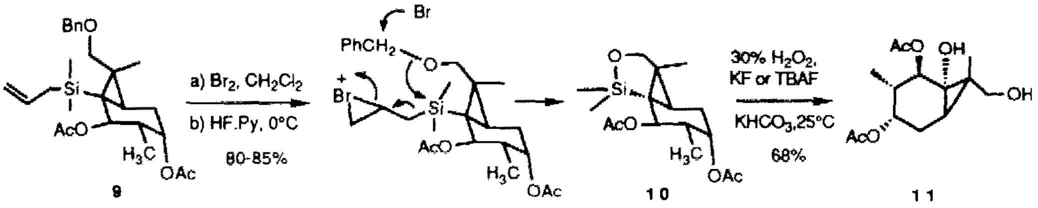
Abstract: The phenyldimethylsilyl to hydroxyl transformation fails in the cases where a cyclic tertiary carbon center is involved as was observed in the synthesis of phorbol C-ring models. An alternate functionality in the form of allyldimethyl silane (ADMS) is found to work well in these and other cases involving tertiary centers. With proper choice of reagents, the ADMS group can be employed as a latent alcohol in systems containing ketones, esters, arenes, and vinyl groups.

Over the last decade, Kumada,[1] Fleming,[2] Tamao,[3] and others have developed versatile sequences for the conversion of carbon-silicon bonds to carbon-oxygen bonds.[4] One of the most common of these processes utilizes the phenyldimethylsilyl (PDMS) functionality, wherein the PDMS to hydroxyl transformation is carried out in either one or two steps, with complete retention of configuration at the carbon to which the the silyl group is attached. However, application of this methodology to execute similar transformations at tertiary carbon centers is rare.[2c] In the course of our synthetic studies with phorbol C-ring model systems, the failure of the attempted PDMS to hydroxyl conversion[5] necessitated the use of an alternate hydroxyl synthon. Herein, we report that allyldimethylsilyl (ADMS) group[6] can successfully serve as a latent hydroxyl group at tertiary carbon centers. The ADMS group is also compatible with a wide variety of functionalities, including ketones, esters, benzylsilanes, vinylsilanes, and simple arylsilanes.

Application of the ADMS moiety for introduction of a tertiary alcohol to a phorbol C-ring model is shown in Scheme I. Treatment of diacetate **4**[7] first with a slight excess of bromine in methylene chloride followed by reaction with pyridinium poly(hydrogen fluoride)[8] provided a 96% yield of the fluorosilane **5**, which can be smoothly oxidized with basic hydrogen peroxide to the corresponding alcohol **6** in 85-95%. In most cases the desired product was isolated as a mixture with a minor amount (5-15%) of the silanol **7**, presumably formed by hydrolysis of the fluorosilane **5**. Product isolation is facilitated by conversion of the alcohol **6** to its acetate **8** (92% yield, 75% overall in 3 steps).



Repetition of the above sequence with the benzyl-protected hydroxymethyl-functionalized ADMS diacetate **9** provided an interesting contrast, providing siloxane **10** in up to 85% yield. Presumably this reaction occurs via oxygen participation during the bromination reaction. The expected benzyl-protected fluorosilane has been synthesized by an alternative method[7] and does not produce cyclic siloxane **10** under the above reaction conditions. Silyl ether **10** could be easily converted into the diol **11** by literature oxidation methods, employing basic hydrogen peroxide in the presence of a fluoride catalyst.[9]



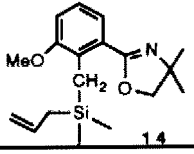
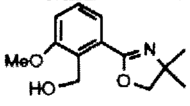
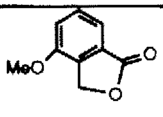
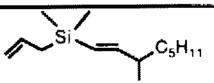
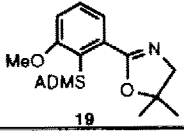
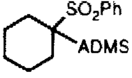
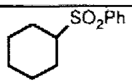
Earlier studies in our laboratory employing the phenyldimethylsilyl group to carry out similar transformations to alcohols were not successful, which could be explained by the fact that the requirement of the ipso-attack[10,4d] poses a difficulty in the phenyl-silicon cleavage in those molecules which have the phenyldimethylsilyl group attached to a tertiary carbon center, since the ipso-addition pathway may be sterically quite demanding. Allylsilanes on the other hand react by an S_E2' type mechanism, and although little work has been expended in comparing the reactivity of allylsilanes and phenylsilanes,[11] preliminary work in our laboratory with allyldimethylphenylsilane **12** demonstrates that the allylsilane functionality is more reactive.

$$\mathrm{PhLi} + \mathrm{ClSiMe_2(CH_2CH{=}CH_2)} \xrightarrow[79\%]{\mathrm{THF},\,-78^\circ\mathrm{C}} \underset{\mathbf{12}}{\mathrm{PhSiMe_2(CH_2CH{=}CH_2)}} \xrightarrow[67\%]{48\%\ \mathrm{HF_{(aq)}},\ \mathrm{CH_3CN}} \underset{\mathbf{13}}{\mathrm{(PhSiMe_2)_2O}}$$

The success of the ADMS to hydroxyl conversion prompted us to briefly survey systems which also contain vinylsilane and benzylsilane functionalities. Thus, when ADMS-benzylsilane **14** was subjected to desilylation-oxidation conditions, either the benzyl alcohol **15** or the lactone **16** was obtained depending on the reaction conditions, the lactone being formed as a consequence of the hydrolysis of the oxazoline moiety by the acetic acid used in the reaction (entries $A_{1,2}$ Table I). Transformation of ADMS-vinylsilane **17** to β-silyloxy aldehyde **18** further illustrates the utility of the method (entry B_1, Table 1).

Limitations to the use of the ADMS to hydroxyl transformation were noted. Treatment of the substrate **19** under various desilylation oxidation conditions afforded a complex mixture (entry C) while the α-ADMS sulfone **20** (entry H) afforded the desilylated phenylsulfonyl cyclohexane **21** as the only product in 75% yield.

TABLE 1.

Entry	Substrate[12]	Conditions	Major product	Yield
A_1	 14	1) KHF_2, CF_3COOH 2) H_2O_2, KF, $KHCO_3$	 15	70%
A_2	**14**	AcOOH, Et_2O, 25°C	 16	91%
B_1	 17	1) KHF_2, CF_3COOH 2) H_2O_2, KF, $KHCO_3$	 18	64%
B_2	**17**	1) Br_2, HF. Py, CH_2Cl_2 1) H_2O_2, KF, $KHCO_3$	**18**	35%
C	 19	1) KHF_2, CF_3COOH, $CHCl_3$ 2) H_2O_2, KF, $KHCO_3$ or AcOOH, Et2O, rt	complex mixture	0%
D	 20	1) I_2, $CDCl_3$, 0°C, aq. workup (→ siloxane, 78%) 2) H_2O_2, KF, $KHCO_3$	 21	75%

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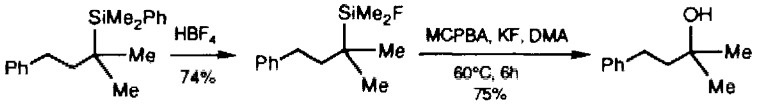

1 **2** **3**

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4) For reviews on organosilanes see: a) Weber, W. P.; "Silicon reagents for Organic Synthesis", Springer-Verlag, 1983; b) Colvin, E. W.; "Silicon in Organic Synthesis", Butterworth, 1981; c) Colvin, E. W.; "Silicon Reagents in Organic Synthesis", Academic Press, 1988; d) Fleming, I.; Chan, T. H. *Synthesis* **1979**, 762. For a review on oxidative cleavage of carbon-silicon bond to carbon-oxygen bond see ref. 3.

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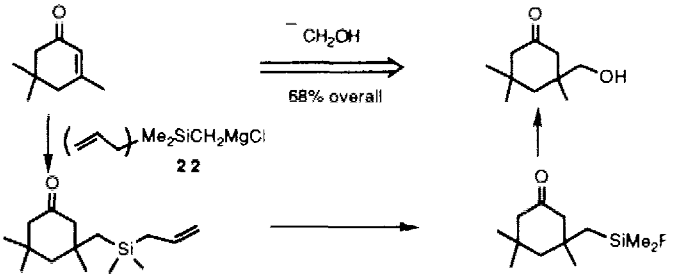

7) Magar, S. S.; Ph. D. Thesis, Purdue University, 1991. Syntheses of compounds **4** and **9** will be described in a subsequent full paper.

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12) All substrates listed in the table were prepared in high yield by quenching the appropriate anion with commercially available (Aldrich Chemical Company) allyl dimethyl chlorosilane.

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