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A NEW REACTION IN ORGANOSILICON CHEMISTRY: THE OXIDATIVE FRAGMENTATION OF γ-HYDROXY SILANES

Stephen R. Wilson*, Paul A. Zucker, Chong-wan Kim and Carmine A. Villa

Department of Chemistry, New York University, Washington Square, New York, 10003

Abstract: The Ce^{+4} fragmentation of γ-hydroxy silanes leads to keto-olefins of predictable structure and stereochemistry.

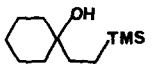
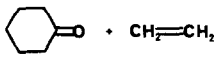
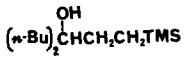
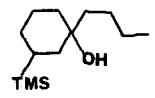
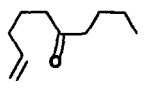
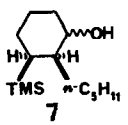
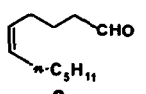
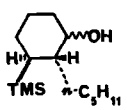
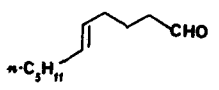
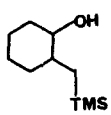
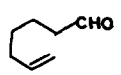
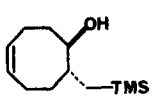
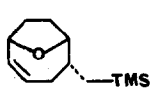
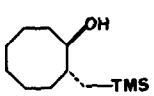
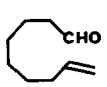
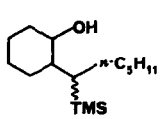
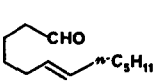
As a consequence of our program to discover new reactions of use in organic synthesis[1] we were intrigued by the reaction shown in equation 1. Trahanovsky[2] reported this single organo-

$$\underset{\mathbf{1}}{PhCHCH_2CH_2TMS}\ (OH) \xrightarrow{(NH_4)_2Ce(NO_3)_6} \underset{\mathbf{2}}{PhCHO} + CH_2{=}CH_2 \qquad (1)$$

silicon example in a 1974 paper on oxidative fragmentations and to our knowledge there have been no subsequent citations.[3] We have used this reaction as a model for our silicon-based enzyme inhibitor[4] chemistry which involves a mechanistically related oxidative cleavage.

While it is well known that β-functionalized silanes are reactive and can be used in organic synthesis, γ-functionalized silanes have found little application. This is evidently due (as pointed out by Fleming) to the fact that the "functional groups are too far away to have an effect on one another."[5] There are, however, a number of ways to prepare γ-functionalized silanes and the remote TMS group would be an ideal latent functionality to carry through a synthesis. We felt therefore that a specific fragmentation reaction of the type in equation 1 would find broad application in organic synthesis. We report here in our preliminary studies of the scope and limitations of the methodology. Our examples also been chosen to emphasize the generality of the reaction and the wide range of routes to γ-hydroxysilanes.

TABLE I. CAN CLEAVAGE OF γ-HYDROXY SILANES[a]

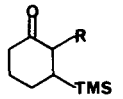
Entry	substrate	product(s)	yield(%)
1			90[b]
2		5-nonanone + $CH_2=CH_2$	39
3	 **6**		66
4	 **7**	 **8**	45[c]
5	 **9**	 **10**	54[d]
6	 **11**		32
7	 **12**		e
8			49
9		 **15**	30

a. 2-8 equivalents CAN in 50% aqueous acetonitrile at 25°C.
b. Based on GC analysis of ethylene.
c. A 42:58 ratio cis/trans was obtained with 8 equivalents CAN, whereas a 75:25 ratio resulted with 20 equivalents.
d. A 85:15 ratio trans/cis was produced with 8 equivalents CAN.
e. A mixture of two isomeric bicyclic ethers were produced.

Entries 1 and 2 serve to only somewhat broaden the scope of Trahanovsky's original reaction. The tert-alcohol in entry 1 was prepared via the addition of β-TMS ethyl Grignard[6] 3 to cyclohexanone while the alcohol in entry 2 arose from n-BuLi addition to the corresponding β-TMS ester 4.[7] The keto-silanes 5a,b were prepared using Still's[8] TMSLi chemistry. Compound 6 (entry 3) is produced by n-BuLi addition to 5a and the subsequent fragmentation proceeds in good yield.

3

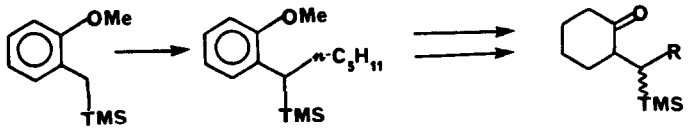
4



5a R = H
5b R = C_5H_{11}

We have applied this chemistry to the synthesis of the major and minor pheromone of the Douglas fir tussock moth.[9,10] Compound 7 and 9 (entries 4 and 5) were prepared from cis or trans 5b respectively. Fragmentation is not stereospecific under our usual reaction conditions, both 7 and 9 giving mainly trans-olefin 10. However, the reaction can be made to be somewhat (75:25) stereoselective at the double bond when a large excess of CAN is used. Under those conditions the intermediate β-silyl radical is oxidized to the β-silyl cation faster than isomerization occurs. Compounds 8 and 10 were then converted to the Tussock Moth pheromones[9] by the addition of n-$C_{10}H_{20}MgBr$ followed by Jones oxidation. Entry 6 was derived using another γ-ketosilane synthesis,[10] alkylation of the metallated imine from cyclohexanone with $ClCH_2TMS$ followed by hydrolysis and LAH reduction. Compound 12 was prepared by addition of $(TMSCH_2)_2CuLi$ to the mono-epoxide of 1,5-cyclooctadiene. Entry 7 produces a failure of the CAN fragmentation, products instead being derived by oxidative addition to the transannular double bond. If the remote double bond is removed by hydrogenation (entry 8) the reaction works well.

Finally, we have developed a totally different γ-ketosilane synthesis (eq. 2) the details of which will be reported elsewhere.



13 14 R = n-C_5H_{11} (2)

Silane 13 can be metallated (HMPA/n-BuLi), alkylated and reduced (Li/NH_3 then H_2/Pd) ultimately to 14. Compound 14 was reduced with LAH and fragmented to produce aldehyde 15 (entry 9).

Clearly a reaction of some generality has been uncovered. We can recommend this

methodology as an excellent alternative to existing cleavage reactions such as the Eschenmoser fragmentation.[11] We are continuing to explore the scope of this process with regards to stereochemistry, mechanism, other oxidants and substrates as well as a number of significant application to natural products synthesis.[12]

REFERENCES AND NOTES

1. This work was supported by NIH Grant GM-31482.
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12. Note added: Since this manuscript was submitted another paper appeared in this journal (Nakatani, K; Isoe, S.; Tetrahedron Lett., 1984, 5335-5338) describing the oxidative fragmentation of γ-hydroxystannanes.

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