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A Direct Conversion of (α-Hydroxyalkyl)silanes to Carboxylic Acids

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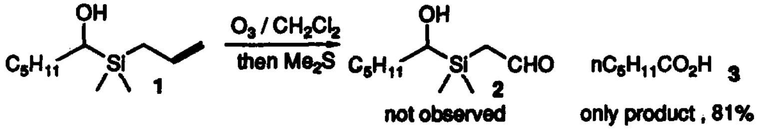
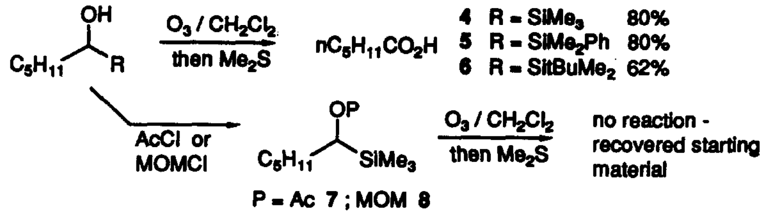
Summary (α–Hydroxyalkyl)trialkylsilanes and acylsilanes are readily oxidized to the corresponding carboxylic acid using ozone.

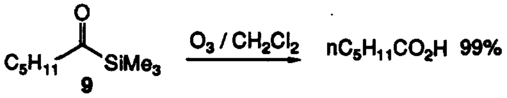
Functionalized silanes such as α-hydroxyalkyl, α-alkoxy[1] and acyl silanes[2] are versatile synthetic intermediates. Acyl silanes may be converted to carboxylic acids under basic oxidizing conditions[2] and to aldehydes under basic conditions[3] or by catalytic reduction.[4] α-Alkoxy silanes are readily transformed to acetals by electrochemical oxidation[1d, 5]. In an attempt to prepare difunctionalized silanes, we have discovered a unique direct oxidation of (α-hydroxyalkyl)trialkylsilanes to a carboxylic acid under mild, neutral conditions using ozone.

(α-Hydroxyhexyl)allyldimethylsilane **1** was prepared by the reverse Brook methodology we reported earlier[6]. Ozonolysis of **1** in CH_2Cl_2 followed by standard reductive work-up using dimethylsulfide did not provide the anticipated aldehyde **2**, but rather hexanoic acid **3** was isolated in 81% yield. We were unaware of any reports concerning this oxidation and sought to probe the scope and limitations as well as the mechanism. In direct analogy with **1**, the trimethylsilyl **4**, dimethylphenylsilyl **5**, and t-butyldimethylsilyl **6** derivatives also provided hexanoic acid upon treatment with ozone in 62-80% yield. Interestingly, when silane **4** was first protected as the acetate **7** or the methoxymethyl ether **8**, the oxidation reaction did not occur. Only unreacted starting material **7** or **8** was recovered with >95% material balance. Therefore, the free hydroxyl group is obligatory for the oxidation while the substituents at silicon seem to have minimal effect other than requiring a



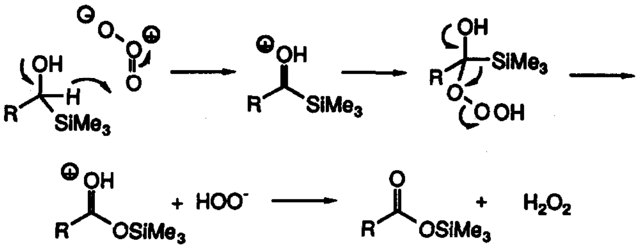


longer reaction time for complete conversion to the acid. Several attempts at carrying out the ozonolysis reaction using **4**, **5** or **6** for short reaction times (30 seconds to 3 minutes) led only to mixtures of hexanoic acid and unreacted starting material. No acyl silane was observed as an intermediate in these incomplete reactions; however, when acyl silane **9** was subjected to ozonolysis in CH_2Cl_2, hexanoic acid was obtained in quantitative yield. This result implies that an acyl silane intermediate may be formed, but would be oxidized at a much faster rate than the (α-hydroxy) silane and therefore would not be observed. Dimethylsulfide does not play a role in the reaction as shown by ozonolysis of **4** in CH_2Cl_2 followed by careful purging of excess ozone with N_2. Analysis of the crude reaction product by GC revealed only the trimethylsilyl ester of hexanoic acid.[7]



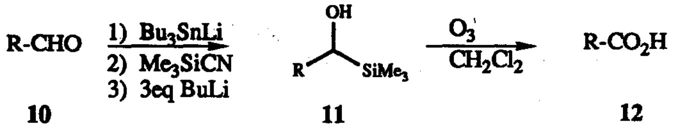
Nucleophilic addition reactions to the carbonyl of acyl silanes with subsequent migration of the silyl group are well known.[2] Diazomethane reacts with acyl silanes to provide either the β-silyl ketone or silyl enol ether derivative dependent upon alkyl or aryl substitution at the carbonyl carbon, respectively. We propose the following mechanism for the oxidation reported herein, see Scheme. An initial ene reaction of the (α-hydroxyalkyl) silane and ozone generates the highly reactive protonated acyl silane which suffers rapid nucleophilic attack at carbon. Migration of the silyl group ultimately releases hydrogen peroxide and the silyl ester after proton transfer. The lack of reactivity of the acetate **7** and ether **8** towards ozone is not readily explained. Although the mechanism of this novel oxidation has not been fully defined, the procedure presented herein provides a useful method for the conversion of functionalized silanes to carboxylic acids.

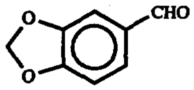
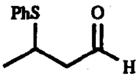
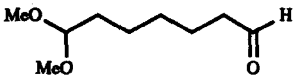
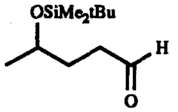
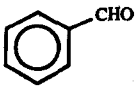
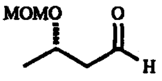
Scheme



The transformation can be carried out in the presence of other non-ozone sensitive functionality including thio ether, acetal, silyl ether and aryl groups, as illustrated in the Table.[8] However, oxygenated aryl rings (such as 3,4-methylenedioxy, entry 1) apparently undergo competitive oxidative fragmentation. We also point out that the synthesis of the (α-hydroxy) silanes **11** by the reverse Brook procedure[6] illustrates that a functionalized aldehyde may be converted to silane **11** in good overall yields. No elimination of β-thiophenol or β-methoxymethyl groups (entries 2 and 6, respectively) was observed at either the nucleophilic addition step or the rearrangement step of the process.

Table Synthesis of (α-Hydroxyalkyl)trimethylsilanes and Subsequent Direct Oxidation to the Corresponding Carboxylic Acid



Entry	Aldehyde **10**	Yield % Silane 11[a]	Yield % Acid 12[b]
1		88	15
2		88	77
3		72	65[c]
4		60	62
5		79	80
6		62	62

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[a] Isolated overall yield from the aldehyde. All new compounds exhibited correct spectral and analytical data. [b] Yield of acid (>95% pure) directly from ozonolysis. [c] Isolated as the methyl ester (reaction of crude acid product with CH_2N_2). Isolation of the acid/acetal resulted in partial hydrolysis of the acetal.

References and Footnotes:

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7. For an example of the conversion of an aldehyde to an ester using ozone, see: Sundararaman, P.; Walker, E. C.; Djerassi, C. *Tetrahedron Lett.* **1978**, *19*, 1627. For ozonolysis of acetals, see: Deslongchamps, P.; Moreau, C. *Can. J. Chem.* **1971**, *49*, 2465.
8. Experimental Procedure:

A solution of the (α-hydroxyalkyl)silane (1 mmol) in 20 mL of CH_2Cl_2 was cooled to -78°C. Ozone was then bubbled through the solution until a blue coloration persisted in the reaction flask (1-5 minutes). The bulkier silanes **5** and **6** required the longer reaction times. Silane **6** was not completely converted to the acid after 5 minutes (~10% remaining starting material). The trimethylsilyl derivatives were generally completely oxidized within 2 minutes. The excess ozone was purged from the reaction vessel using N_2 and dimethylsulfide (2 mmole) was then added (as a precaution to ensure complete removal of excess ozone). The mixture was allowed to warm to room temperature and then washed with satd. sodium bicarbonate (2x20mL). The aqueous phase was acidified (1N HCl) and extracted with ether (3x30mL). The combined organic fractions were dried over $MgSO_4$ and the solvent then removed under reduced pressure to provide the acid in >95% purity.

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