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Regioselective Oxidative Cleavage of Functionalized Unsymmetric Tetraalkylstannanes via Ozone

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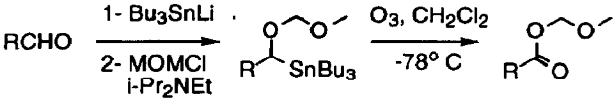
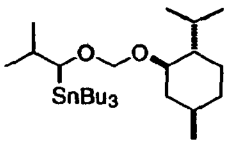
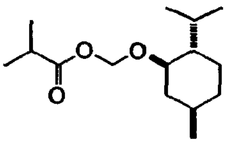
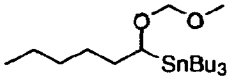
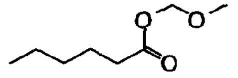
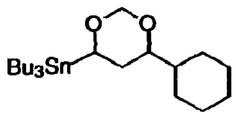
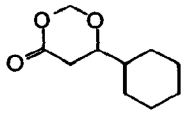
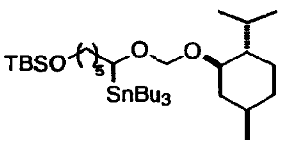
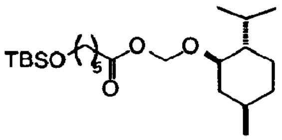
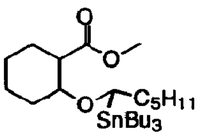
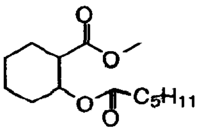
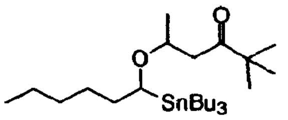
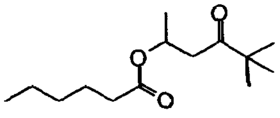
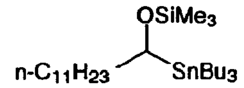
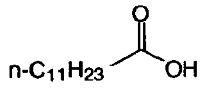
Abstract: The direct oxidation of (α-alkoxyalkyl)trialkylstannanes to esters by reaction with ozone is described.

The regioselective oxidative cleavage of carbon tin bonds is a potentially very useful synthetic process, yet few methods have been developed for this transformation. Conversion of a non-symmetric tetraalkyl stannane to a carbonyl using Collins reagent [1] or to a dimethyl acetal upon reaction with ceric ammonium nitrate in methanol [2] has been reported. A two step procedure for the conversion of the tributylstannyl moiety to an alcohol with retention of configuration has also been developed. [3] β-Stannyl cycloalkanones undergo a tin directed Baeyer-Villager reaction upon treatment with m-chloroperbenzoic acid, resulting in an alkene ester, [4] while treatment of β-tributylstannyl cycloalkanols with iodosobenzene results in ring opened keto alkenes. [5] An oxidative fragmentation can also be achieved on cyclic hemiacetals [6] or β-tributylstannyl oximes. [7] We recently reported the regioselective oxidative cleavage of an (α-hydroxyalkyl)trialkylsilane to a carboxylic acid using ozone. [8] The use of ozone to oxidize tetraalkylstannanes and silanes has been studied in some detail; however, there has been no development of this reaction into a practical synthetic method. [9] We wish to report here our findings on the regioselective oxidative cleavage of (α-alkoxyalkyl)trialkylstannanes by ozone. The overall reaction represents an efficient conversion of an aldehyde to an ester under mild reaction conditions.



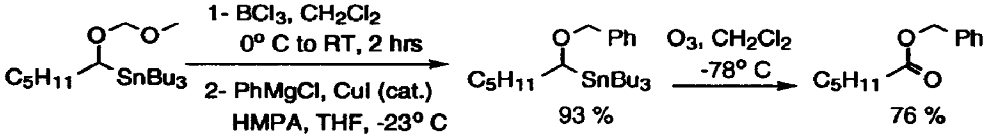
Oxidative cleavage of an (α-hydroxyalkyl)trialkylstannane was expected to lead to formation of the corresponding carboxylic acid in direct analogy to the silane example noted previously. [8,10] Surprisingly, this reaction did not generate the anticipated product, but rather led to a complex mixture of decomposition products which were not characterized. Interestingly, upon treatment of the methoxymethyl (MOM) ether derivative of the (α-hydroxyalkyl)trialkylstannane, the ester was obtained in excellent yield. In subsequent experiments, we have determined that the oxidative cleavage of (α-alkoxyalkyl)trialkylstannanes to the corresponding ester is a general reaction, see Table. The free acid can be obtained if the ozonolysis reaction is carried out on an (α-silyloxyalkyl)trialkylstannane [11] followed by work-up with dilute aqueous acid, see Table entry 7.

Table. Oxidative Cleavage of Tetraalkylstannanes with Ozone

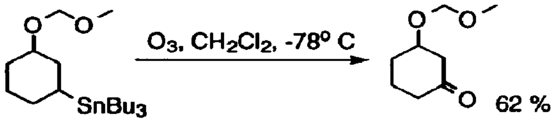
Entry	Stannane	Carbonyl Product [a]	% Yield [b]
1			91
2			100
3			83
4			91
5			92
6			100
7	 $n\text{-}C_{11}H_{23}CH(OSiMe_3)SnBu_3$	 $n\text{-}C_{11}H_{23}COOH$	74

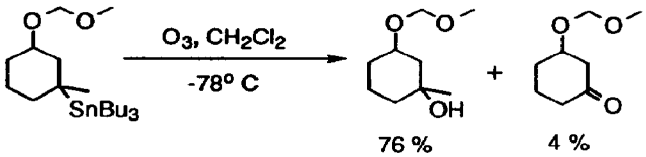
[a] All new compounds were fully characterized. [b] Isolated yields.

The role of the second oxygen atom in the alcohol protecting group was examined by the preparation of the benzyl ether derivative. Direct benzylation of an (α-hydroxyalkyl)trialkylstannane did not result in acceptable yields of the benzyl ether. Conversion of the MOM protecting group to the benzyl group was then accomplished by the sequence shown below. Regioselective cleavage of the MOM acetal was achieved by treating the acetal with boron trichloride. The intermediate α-chloro ether was surprisingly stable. Addition of phenyl Grignard in the presence of a catalytic amount of copper iodide then provided the benzyl ether in 93% overall yield. This method has also proven to be a general procedure for the conversion of MOM protected (α-alkoxyalkyl)trialkylstannanes to other ethers. [12] Ozonolysis of the benzyl ether resulted in the benzyl ester in 76% yield, indicating that the acetal protecting group is not a requirement for the regioselective oxidative cleavage of the stannane.

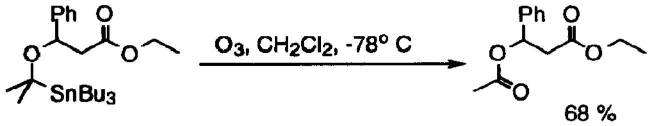


The importance of the adjacent alkoxy group in the ozonolytic cleavage was then examined. Tributyltinlithium was added to cyclohexenone and 3-methylcyclohexenone to provide the corresponding 3-tributylstannyl cyclohexanone derivatives. [1] Reduction of the ketone ($NaBH_4$) was followed by protection of the alcohol as the methoxymethyl ether. Ozonolysis of the secondary cyclohexylstannane resulted in a 62% yield of 3-(methoxymethoxy)cyclohexanone, while oxidative cleavage of the tertiary substituted stannane derivative provided a 76% yield of the tertiary alcohol and 4% of the ketone resulting from loss of the methyl group.





Clearly the (α-alkoxy)alkyl group is not required. However, it is important to note that the cyclohexane portion of the molecule is obtained as the oxidized product preferentially. [13] Neither butyric acid, butanal, nor butanol were observed (by GC analysis of the crude reaction mixture) in any of the stannane ozonolysis reactions. The reaction produces a white solid which may be a polymeric dibutyltin oxide (MS, NMR) as reported earlier for symmetric tetraalkylstannanes. [9] Aleksandrov and Tarunin [9a] have proposed a mechanism which involves the addition of ozone to the tin atom followed by migration of an alkyl group to the terminal oxygen. Subsequent decomposition of the stannyl hydroperoxide intermediate by hydrogen transfer then results in the oxidized product. In the reaction of (α-alkoxyalkyl)trialkylstannanes, the oxygen substituted alkyl group migrates preferentially. In the example of a secondary alkyl substituted stannane, hydrogen transfer then results in the ester or ketone. The tertiary alkyl substituted stannane results in an additional product arising from a second migration of the methyl group. The subsequent cleavage of an alkyl group from a tertiary alkyl substituted stannane derivative proved to not be an isolated case. Indeed, the tertiary substituted aldol derivative shown below also undergoes oxidation and fragmentation to provide the acetate derivative. This route therefore



provides a mild method for the selective removal of the stannyl moiety from the stereoselective mixed stannyl substituted acetal aldol reaction we reported earlier. [14]

In summary, we have determined an efficient method for the oxidative cleavage of unsymmetric tetraalkylstannanes under very mild conditions. [15] Acetals, benzyl ethers, and phenyl functional groups are compatible under the reaction conditions. The methodology provides a useful route for the conversion of stannanes to ketones or alcohols in excellent yield. The overall process provides a new route for the conversion of aldehydes to esters. Further investigation of the utility and mechanism of this process are underway.

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References and Footnotes

1. Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836-4838.
2. (a) Hanessian, S.; Leger, R. *J. Am. Chem. Soc.* **1992**, *114*, 3115-3117. (b) Hanessian, S.; Leger, R. *Synlett* **1992**, 402.
3. Herndon, J. W.; Wu, C.; Harp, J. J. *Organometallics* **1990**, *9*, 3157-3171.
4. Bakale, R. P.; Scialdone, M. A.; Johnson, C. R. *J. Am. Chem. Soc.* **1990**, *112*, 6729-6731.
5. Ochiai, M.; Ukita, T.; Iwaki, S.; Nagao, Y.; Fujita, E. *J. Org. Chem.* **1989**, *54*, 4832-4840.
6. (a) Ochiai, M.; Ukita, T.; Nagao, Y. *Chem. Lett.* **1987**, 133-136. (b) Posner, G. H.; Webb, K. S.; Asirvatham, E.; Jew, S.-S.; Degl'Innocenti, A. *J. Am. Chem. Soc.* **1988**, *110*, 4754-4762.
7. Nishiyama, H.; Arai, H.; Ohki, T.; Itoh, K. *J. Am. Chem. Soc.* **1985**, *107*, 5310-5312.
8. Linderman, R. J.; Chen, K. *Tetrahedron Lett.* **1992**, *33*, 6767-6770.
9. (a) Aleksandrov, Y. A.; Tarunin, B. I. *Russ. Chem. Rev. (Engl. Trans.)* **1977**, *46*, 905-914. (b) Tarunin, B. I.; Tarunina, V. N.; Aleksandrov, Y. A. *Zh. Obshch. Khim. (Engl. Trans.)* **1982**, *52*, 2027-2029.
10. (α-Heteroatom) substituted stannanes have also been oxidatively cleaved to a radical or carbocation by electrochemical methods: (a) Yoshida, J-I.; Ishichi, Y.; Nishiwaki, K.; Shiozawa, S.; Isoe, S. *Tetrahedron Lett.* **1992**, *33*, 2599-2602. (b) Yoshida, J-I.; Ishichi, Y.; Isoe, S. *J. Am. Chem. Soc.* **1992**, *114*, 7594-7595. (c) Yoshida, J-I.; Itoh, M.; Isoe, S. *J. C. S., Chem. Comm.* **1993**, 547-549. (d) Narasaka, K.; Kohno, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3456-3463. The oxidation of tetraalkylstannanes to provide alkyl radicals has also been examined: (e) Wong, C. L.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 5593-5603. (f) Rollick, K. L.; Kochi, J. K. *J. Am. Chem. Soc.* **1982**, *104*, 1319-1330. (g) Lochynski, S.; Boduszek, B.; Shine, H. J. *J. Org. Chem.* **1991**, *56*, 914-920.
11. Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392-2398.
12. R. J. Linderman, S. Chen, M. Jaber, unpublished results.
13. Cleavage of unsymmetric tetraalkylstannanes by electrophilic attack of bromine is selective for the least substituted ($1^{o}>2^{o}>3^{o}$) alkyl group, see: (a) Gielen, M. *Acc. Chem. Res.* **1973**, *6*, 198-202. (b) Antonsen, O.; Bennecke, T.; Gunderson, L. L.; Undheim, K. *Acta Chem. Scand.* **1992**, *46*, 172-177.
14. Linderman, R. J.; Anklekar, T. V. *J. Org. Chem.* **1992**, *57*, 5078-5082.
15. General procedure: The stannane (0.3mmol) was dissolved in CH_2Cl_2 (5 mL) and cooled to -78°C. Ozone was bubbled through the solution until a blue color persisted in the reaction flask. Ar gas was then bubbled through the solution for five minutes to dispel excess ozone, and the reaction mixture was allowed to warm to room temperature. The solvent was removed under reduced pressure and the crude product purified by chromatography (SiO_2) using ethyl acetate/hexanes as eluent. The reaction has been carried out on scales up to 500 mg without any reduction in the yield of the ester. The acid (entry 7) is obtained by dissolving the crude product in ether, washing with sat'd aqueous $NaHCO_3$, and then acidifying the aqueous phase with 2N HCl.

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