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OXIDATIVE FRAGMENTATION OF γ-HYDROXYALKYL STANNANES STEREOSPECIFIC FORMATION OF (E) AND (Z)-KETO OLEFINS

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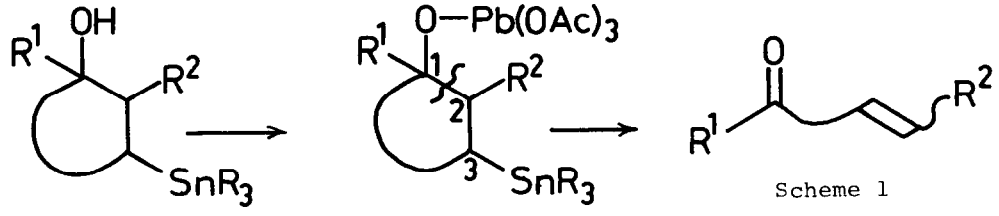
Summary; Treatment of γ-hydroxyalkyl stannanes with lead tetraacetate in refluxing benzene leads to the stereospecific formation of (E) and (Z)-keto olefins according to the stereochemistry of the starting materials in excellent yield.

The reactions involving selective carbon-carbon bond cleavage in cyclic compounds constitute important methodologies in synthetic organic chemistry. In spite of many reports of 1,4-fragmentation such as Grob fragmentation[1] which employ electron accepting groups as the leaving gruop (an anion induced fragmentation), few example which employ electron donating groups as the leaving group (cation or radical induced fragmentations) have been reported up to now.[2] Here we wish to report an oxidative fragmentation of γ-hydroxyalkyl stannanes with lead tetraacetate (LTA) to afford keto olefins with stereospecific manner.[3),4]

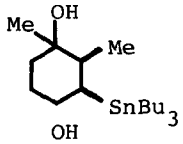
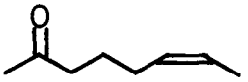
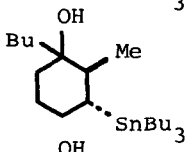
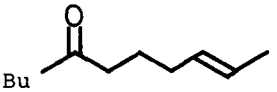
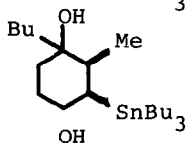
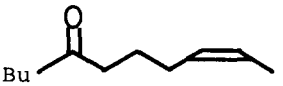
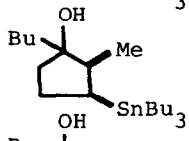
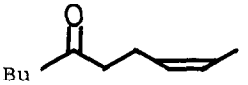
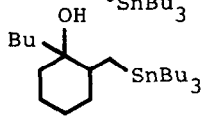
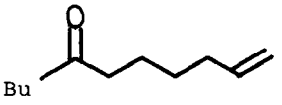
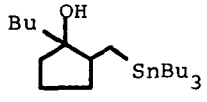
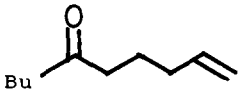
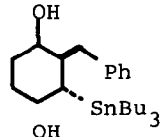
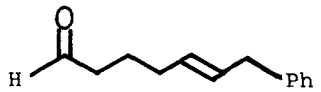
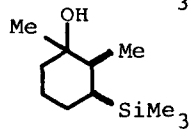
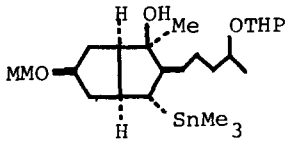
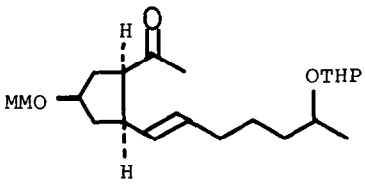
The transformation in scheme 1 will be envisioned if a substituent on C3 can not only stabilize a cation or a radical on C2, generated by the C1-C2 bond cleavage with an appropriate oxidizing agent, but also successively induces facile elimination to afford an olefin. Organostannane substituents seem to satisfy these requirements because they stabilize β-cation or radical species through σ-π conjugation and undergo spontaneous elimination to form the corresponding unsaturated organic compounds.[5] For this purpose LTA seems to be the suitable oxidizing agent, because the alkoxy radical is generated by the O-Pb bond cleavage of initially formed alkoxy lead species by heat or light.[6]



Scheme 1

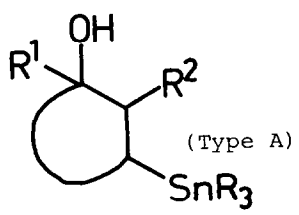
The starting materials, γ-hydroxyalkyl stannanes, were prepared by alkylation of the corresponding γ-ketostannanes which were obtained by conjugate

Table 1. Oxidative fragmentation of γ-hydroxyalkyl stannanes with lead tetraacetate.

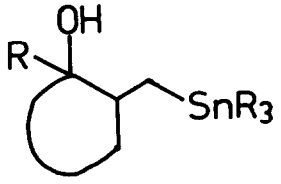
Entry	γ-Hydroxyalkyl stannane		Product		Yield
1		1		2	69%
2		3		4	95%
3		5		6	91%
4		7		8	84%
5		9		10	91%
6		11		12	81%
7		13		14	77%[a]
8		15			
9		16		17	76%[b]

Footnotes a) purified by silica gel column chromatography.
b) calcium carbonate (1eq) was added.

addition of Bu_3SnLi to α,β-unsaturated ketones[7] (Type A) or alkylation of lithio enamines of cyclic ketone with ICH_2SnBu_3[8] (Type B).



(Type A)

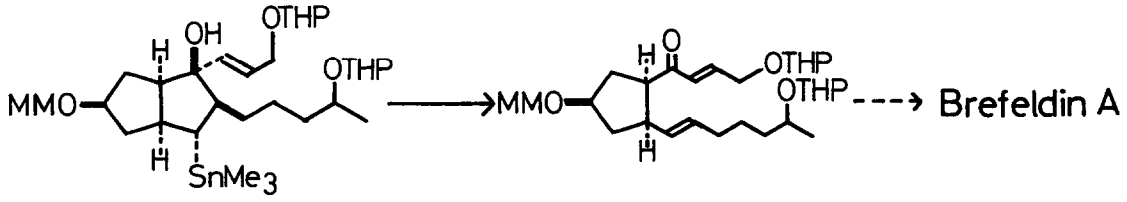


(Type B)

A typical experimental procedure is as follows.
To a suspension of LTA (253mg, 0.6mmol) in dry refluxing benzene (1 ml), hydroxy stannane 3 (entry 2)(227mg, 0.5mmol) in dry benzene (4 ml) was added, and the whole was refluxed for 5 minutes. Aqueous workup ($NaHCO_3$, 1N-HCl) and purification by alumina column chromatography gave (E)-2-undecene-7-one 4 (79mg) in 95% yield.

Trans 3 and cis 5 isomers undergo the fragmentation stereospecifically to afford (E) and (Z)-2-undecene-7-one, respectively.[9] This observed stereospecificity in the internal olefin formation in these cases can be accounted by anti-elimination. Terminal olefins were also obtained from type B γ-hydroxyalkyl stannanes in good yield (entry 5,6). Even the secondary alcohol derivative of γ-hydroxyalkyl stannane 13 (entry 7) readily reacted with LTA to afford unsaturated aldehyde 14 in 77% yield without formation of corresponding γ-ketostannane.[10] However γ-hydroxyalkyl silane 15[11] (entry 8) which employed Me_3Si group instead of Bu_3Sn group of compound 1 did not react with LTA under same conditions. Additional examples are also summarized in table 1.[12]

This fragmentation was applied to the key step of our total synthesis of (±)-Brefeldin A[13] from the useful and versatile synthetic intermediate, a bicyclo-[3,3,0]-octane derivative.[14] α,β-Unsaturated ketone 19 was obtained by the reaction of allylalcohol 18 with LTA in 82% yield. The conversion of 19 to Brefeldin A is now under investigation.



18 19

Acknowledgment; We thank Dr. Motokazu Uemura for making a chance to study organostannane chemistry and his useful suggestions, active discussions, and encouragement.

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