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α-Alkoxystannyl Ethers In Organic Synthesis: Synthesis of Functionalised γ-Butyrolactones

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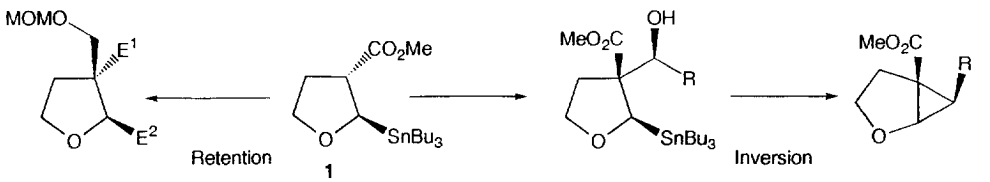
Abstract: Ozonolysis of a variety of (tetraydrofuran-2-yl)tri-n-butylstannanes affords the corresponding γ-butyrolactones in good to excellent yields. This reaction is tolerant to a range of other functional groups and provides access to substituted γ-butyrolactones not available from aldol reactions of the parent lactone.

Recently we demonstrated that the trialkylstannyl group in the readily available tetrahydrofuran **1**[1] serves as a removable stereocontrol element for the preparation of 2,3- disustituted[2] and 2,3,3-trisubstituted[3] tetrahydrofurans. The tin moiety also behaves as a sterically demanding substituent in the enolisation of the ester group, controlling enolate geometry and thereby influencing the stereochemical outcome of the aldol reactions[4,5] of **1**. Thus far we have concentrated upon alkylation strategies for the unmasking of the carbon - tin bond, the stereochemical outcome of which depends upon the nature of the substrate and reaction conditions employed, [2,3,6] **Scheme 1**. In this *Letter* we report a facile oxidative functionalisation of the these stannanes which affords rapid access to a variety of γ - butyrolactones.



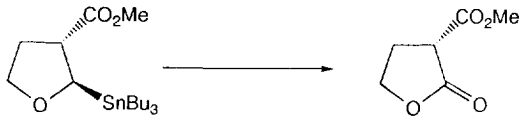
Scheme 1

Initial attempts to effect oxidation of stannanes such as **1** focused upon the methodology developed by Still[7] which utilises chromium (VI) regents. For example, treatment of the stannane **2** with CrO_3 - pyridine in CH_2Cl_2 (10 eq.; 20 °C; 9 hrs.) afforded the lactone **3** in 26% isolated yield. In contrast oxidation of the ester **1** using the same procedure was wholly unsatisfactory, affording the lactone **4** in only trace amounts (4% isolated yield),

Scheme 2. Nevertheless we were encouraged by these results and a variety of oxidising agents were screened[8] in order to optimise this transformation. After some experimentation we adopted the procedure developed by Linderman,[9] which utilises ozone as the oxidising agent, and were pleased to find that this procedure proved to be very general and tolerant of a number of other functional groups, **Table**.

2 3

Conditions: CrO_3 /pyridine; CH_2Cl_2, 9 hrs. (26%)



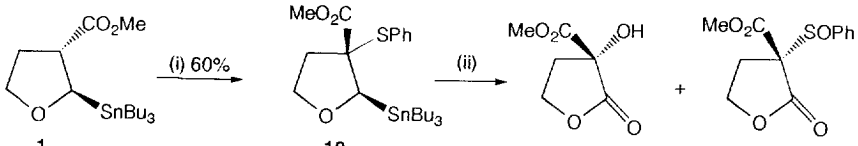
1 4

Conditions: CrO_3 /pyridine; CH_2Cl_2, 9 hrs. (4%)

O_3, CH_2Cl_2; -78 °C (63%)

Scheme 2

We have shown during the course of our initial studies that this oxidation sequence is compatible with a number of other functional groups:- acetonide[10] (*e.g.* substrates **5**), ester (*e.g.* substrates **1** and **7**), ketone (substrate **17**) and unprotected hydroxylic functionality (substrates **9**, **11** and **13**), **Table**. Oxidation of the acetal **15** also proceeds smoothly and is not hampered by competing oxidation of the doubly activated acetal C-H bond. Direct comparison of the chromium and ozonolysis protocols, as in the case of the ester **1**, clearly underscores the advantages of the ozonolysis procedure, **Scheme 2**. In a more demanding test of the chemoselectivity of this lactone synthesis, oxidation of the readily available sulfide **19** was next attempted. Unfortunately, exposure of a solution of **19** in CH_2Cl_2 at -78 °C to ozone as above resulted in a complex reaction mixture from which the hydroxy-lactone **14** and the sulfoxide-lactone **20** were isolated in low yield (*c.a.* 10%), **Scheme 3**.



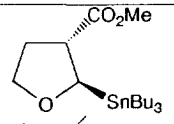
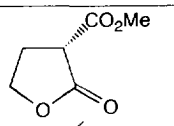
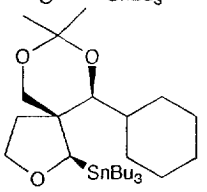
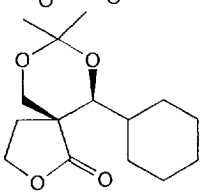
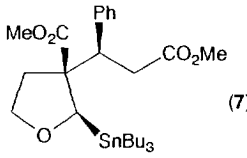
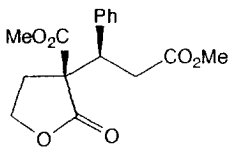
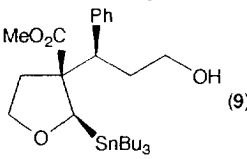
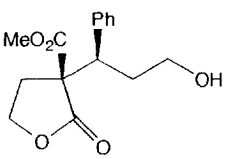
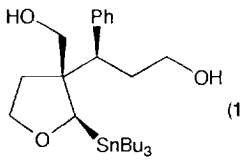
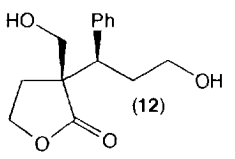
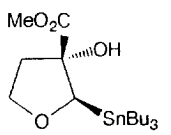
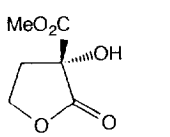
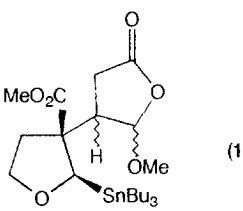
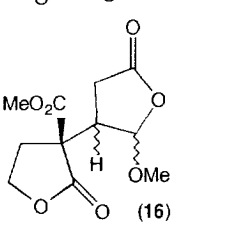
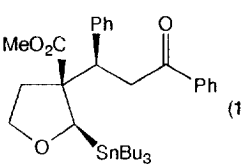
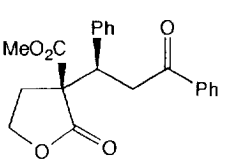
1 19 14 20

Reagents and conditions: (i) a. LDA, THF, -78°C; b. $PhSSO_2Ph$, THF, -78 °C; (ii) O_3, CH_2Cl_2, -78 °C

Scheme 3

One synthetic advantage of this chemistry is that aldol derivatives such as **21** become readily available *via* the stannane **1**. Intermediates such as **22** are not directly accessible from the aldol reactions of the lactone **4** itself due to the reversible nature of this particular reaction. Indeed, ozonolysis of the tin - aldol product **23** resulted in the isolation of the lactone **4** presumably *via* a retro - aldol reaction, **Scheme 4**.

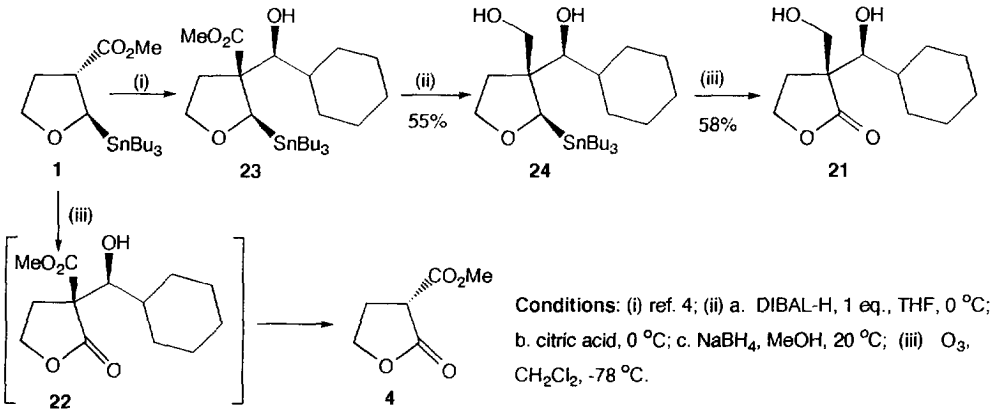
Table: Ozonolysis of Stannanes*

Stannane	Lactone (); (% yield)
 (1)	 (4) (63%)
 (5)	 (6) (31%)
 (7)	 (8) (67%)
 (9)	 (10) (68%)
 (11)	 (12) (72%)
 (13)	 (14) (63%)
 (15)$	 (16) (68%)$
 (17)	 (18) (83%

* All ozonolysis experiments were conducted in CH_2Cl_2 at -78 °C. Yields refer to isolated products after column chromatography. $ Single diastereoisomer.

General Experimental Procedure

The following procedure is representative. Stannane **1** (130 mg, 0.31 mmole) was dissolved in CH_2Cl_2 (5 ml) and the solution cooled to -78 °C. Ozone gas was bubbled through the solution until a faint blue colour was observed. The reaction mixture was purged with dinitrogen and concentrated *in vacuo*. Flash chromatography of the residue afforded the lactone **4** as a viscous oil, yield 28 mg (63%).



Scheme 4

Acknowledgements

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8. For leading references see Coldham, I.; Hufton, R. *Tetrahedron Letters*, **1995**, *36*, 2157.
9. Linderman, R. J.; Jaber, M.; *Tetrahedron Letters*, **1994**, *35*, 5993.
10. All new compounds were fully characterised by ^1H nmr, ^{13}C nmr, ir, high resolution mass spectrometry and/or combustion microanalysis. The synthesis of **5**, **7**, **9**, **11**, **13**, **15** and **17** will be described elsewhere (M. L. Lewis, Ph.D Thesis, University of Manchester 1995; P. Gilbert and P. Quayle, Unpublished results).

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