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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. Copyright © 1996 Elsevier Science Ltd

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- disustituted² and 2,3,3-trisubstituted³ 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.





Initial attempts to effect oxidation of stannanes such as 1 focused upon the methodology developed by Still⁷ 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 screened⁸ 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**.



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:- acetonide¹⁰ (*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.



Reagents and conditions: (i) a. LDA, THF, -78°C; b. PhSSO₂Ph, THF, -78 °C; (ii) O₃, CH₂Cl₂, -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*

* All ozonolysis experiments were conducted in CH₂Cl₂ 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%).





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- All new compounds were fully characterised by ¹H nmr, ¹³C 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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