Anomeric Oxygen to Carbon Rearrangements of Alkynyl Tributylstannane Derivatives of Lactols.

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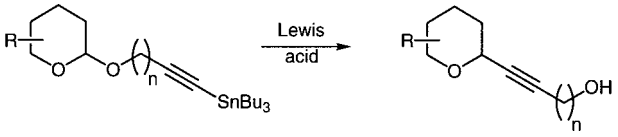
Abstract: Treatment of alkynyl tributylstannane tetrahydropyranyl and tetrahydrofuranyl ether derivatives with boron trifluoride etherate effects an efficient anomeric oxygen to carbon rearrangement leading to the corresponding carbon-linked alkynol products.

The overwhelming abundance of naturally occurring products containing carbon-linked tetrahydropyranyl and tetrahydrofuranyl heterocycles has inspired the development of methodology for their synthesis, especially over the past two decades.[1]

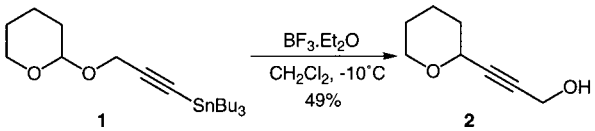
In a recent communication we have described a new route to 2-alkyl substituted pyran derivatives starting from readily prepared tetrahydropyranyl ether derivatives of a variety of alkenols, under mild conditions and in high yield.[2] Prior to this work, a few examples of this type of rearrangement had been reported for vinylic,[3] phenolic[4] and allylic[5] ether systems. However, the potential of a *general* anomeric oxygen to carbon rearrangement using a wider range of more synthetically useful nucleophiles has remained largely unexplored.

In this communication we wish to report the reaction of alkynyl stannanes as the nucleophilic carbon component in the rearrangement sequence. Alkynyl stannanes have been used previously in an intermolecular fashion to displace anomeric halides.[6] Their ease of preparation and handling, combined with their inherent reactivity towards oxonium ion intermediates, made this group ideally suited to the rearrangement protocol (Scheme 1).



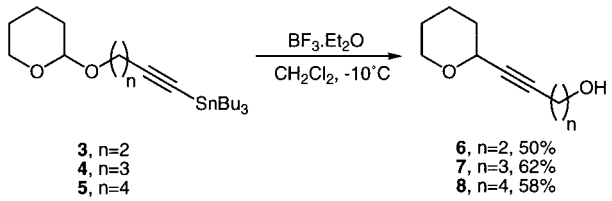
Scheme 1

In our initial investigations commercially available tetrahydropyranyl propargylic ether was stannylated using butyllithium and tributyltin chloride following standard procedures to give **1**. The rearrangement of the alkynyl tributylstannane **1** was then investigated using a range of solvents, concentrations, temperatures and Lewis acids. The optimal conditions for the reaction required a concentrated solution of the alkynyl stannane **1** in dichloromethane at -10°C using boron trifluoride etherate as the mediator for the transformation. Simple aqueous work up and purification by column chromatography afforded the carbon linked product **2** in acceptable chemical yield (Scheme 2).



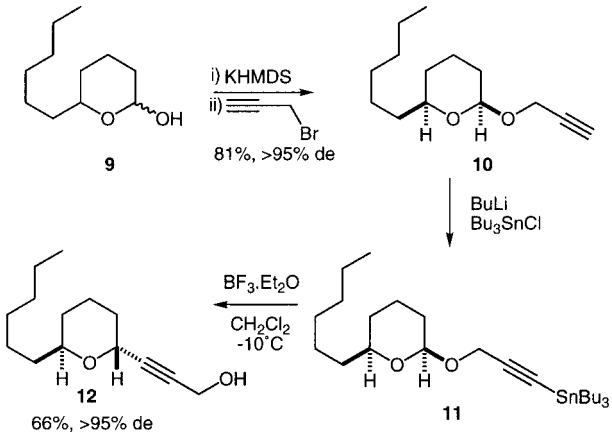
Scheme 2

Application of these best conditions to a series of readily prepared homologated alkynyl stannanes **3**-**5**, lead in each case, to the carbon-linked products **6**-**8** in moderate to good yields (Scheme 3).



Scheme 3

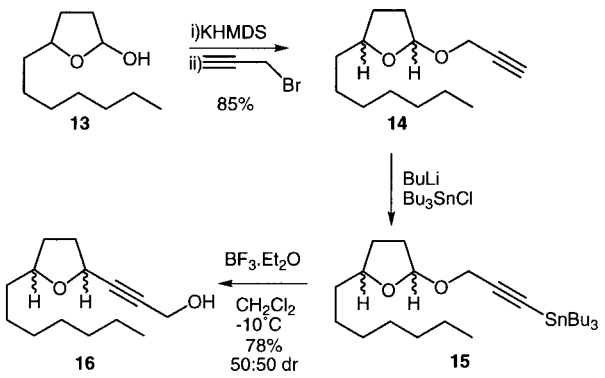
In further studies we investigated the rearrangement of 6-substituted tetrahydropyranyl ether derivative **11**. The alkyne precursor to this material was readily prepared as a single diastereoisomer through alkylation of lactol **9** with propargyl bromide using potassium bis(trimethyl)silylamide in tetrahydrofuran at room temperature. Stannylation of **10** following the usual procedures afforded crude **11** upon work up, which was subsequently treated with boron trifluoride etherate in dichloromethane at -10°C. Work up and purification afforded the desired alkynol product **12** in high yield and as a single diastereoisomer (Scheme 4).[7]



Scheme 4

In a similar fashion the tetrahydrofuranyl propargylic ether **14** was readily prepared by alkylation of lactol **13** with propargyl bromide. Tributylstannylation of this material and subsequent treatment of **15** with boron trifluoride etherate under the usual conditions lead to the desired carbon linked product **16** as a 50:50 mixture of diastereoisomeric products at the newly formed stereogenic centre (Scheme 5).

We believe that the anomeric oxygen to carbon rearrangement described above for alkynyl tributylstannanes will be of great utility in the synthesis of naturally occurring and biologically important compounds. In addition, due to the ready preparation of both **12** and **16** from the requisite lactols through alkylation with propargyl bromide and subsequent rearrangement, we feel that the sequences represented in schemes 4 and 5 constitute a useful tool in anomeric carbon-carbon bond formations with potential application in natural product synthesis.



Scheme 5

Acknowledgements. We thank the EPSRC (to EWT and DJD) and the Novartis Research Fellowship (to SVL) and Pfizer inc. Central Research Division, Groton, U.S.A. for financial support.

References and Notes

(1) For excellent reviews see: i) Levy, D.; Tang, C. *The Chemistry of C-Glycosides*, Pergamon, **1995**; ii) Postema, M. H. D. *Tetrahedron*, **1992**, *48*, 8545, and references cited therein.

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(4) For examples of aryl O- to C- anomeric rearrangements see: i) Ramesh, N. G.; Balasubramanian, K. K. *Tetrahedron Lett*., **1992**, *33*, 3061; ii) Casiraghi, G.; Cornia, M.; Rassu, G.; Zetta, L.; Fava, G. G.; Belicchi, M. F. *Tetrahedron Lett.*, **1988**, *29*, 3323; iii) Casiraghi, G.; Cornia, M.; Rassu, G.; Zetta, L.; Fava, G. G.; Belicchi, M. F. *Carbohydrate Res*., **1989**, *191*, 243.

(5) For examples see: i) Herscovici, J.; Delatre, S.; Antonakis, K. *J. Org. Chem*., **1987**, *52*, 5691; ii) Mikami, K.; Kishino, H.; *Tetrahedron Lett.*, **1996**, 37, 3705.

(6) Zhai, D.; Zhai, W.; Williams, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 250.

(7) Selected spectroscopic data for **12**: ^{1}H NMR (400MHz, $CDCl_3$): 4.77 (d, J = 1.77 Hz, 1H, OC<u>H</u>C≡C), 4.32 (d, J = 4.4 Hz, 2H, C<u>H</u>$_2$OH), 3.76-3.80 (m, 1H, CH_2C<u>H</u>$(CH_2)O$), 1.15-1.90 (m, 16H, 8xC<u>H</u>$_2$), 0.87 (t, J = 6.3 Hz, 3H, C<u>H</u>$_3$); ^{13}C NMR (100MHz, $CDCl_3$): 84.6, 84.3 (OCHC≡<u>C</u> and OCH<u>C</u>≡C), 71.8 (CH_2<u>C</u>H$(CH_2)O$), 65.0 (O<u>C</u>HC≡C), 51.2 (<u>C</u>H$_2$OH), 36.1, 31.8, 31.3, 30.5, 29.3, 25.3, 22.6, 19.4 (8x<u>C</u>H$_2$), 14.0 (<u>C</u>H$_3$). The *trans* geometry of **12** was confirmed by nOe experiments.