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THE REACTION OF BIFUNCTIONAL ANNULATING REAGENTS WITH CYCLIC ENOL ETHERS: A NEW ROUTE TO FUSED CYCLIC ETHERS

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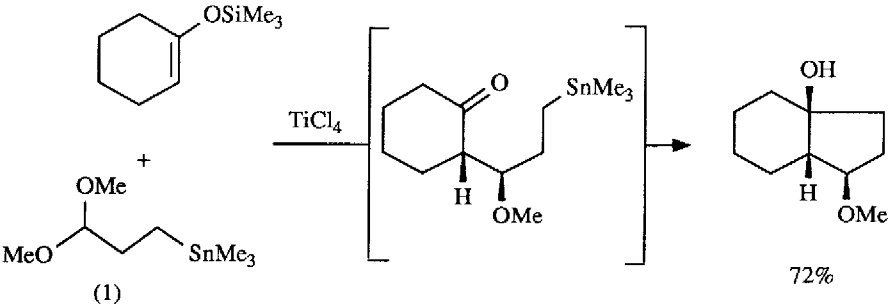
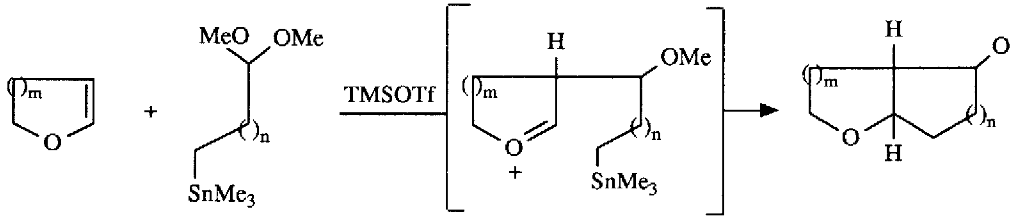
Summary:- The acetal-stannane (1) and its two higher homologues react with cyclic enol ethers, including those derived from sugars, to provide ready access to fused cyclic ethers.

We have recently introduced organotin compounds such as (**1**) for use in a [3+2] annulation reaction of O-silylated enolates[1]. Such reactions of bifunctional species offer real advantages for the rapid and efficient preparation of carbocyclic systems, as well as being inherently interesting with respect to the chemoselectivity they display. It was thus of value to see if we could extend the mode of reaction of these compounds to a reaction with cyclic enol ethers so giving a new and possibly efficient synthesis of ring fused cyclic ethers. The continuing interest in the chemistry of natural compounds in which cyclic ether structural units occur, and a recent disclosure on the reaction of cyclic enols with acetals[2] prompt us to report on our success in extending the chemistry of these novel annulation reactions.



The reaction of (1) with cyclic ethers and trimethylsilyl trifluoromethanesulphonate (TMSOTf) forms the oxonium ion (**2**) via nucleophilic attack of the enol at the electrophilic acetal centre. The inherent electrophilicity of oxonium species means that no other Lewis acids are required, and ring closure to form a fused cyclic ether occurs. A consequence of this is that the two higher homologues of (**1**) can be used in this reaction to form six and seven-membered fused ring systems. Previous attempts to utilise these compounds failed due to their requiring stronger Lewis acids than TMSOTf when they undergo a preferential β-elimination reaction[3]. Although we have isolated intermediate acetals from these reactions, formed by trapping of (**2**) with TMSOMe generated from the acetal (**1**) and TMSOTf, they too cyclize rapidly to the products in the presence of a slight excess of TMSOTf.



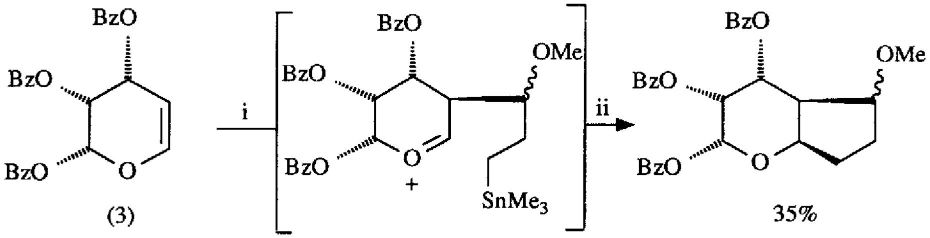
(2)

Entry	m	n	% Yield[a]
1	1	1	60
2	1	2	56
3	1	3	48
4	2	1	69
5	2	2	46
6	2	3	44

a) Combined yield of all diastereoisomers from reactions with $AlCl_3$.

The stereochemical outcome of the reaction follows that observed in our previous studies with the first step showing a dependence upon the Lewis acid used[4]. Thus TMSOTf gives a 70:30 mixture of *l* to *u* isomer, whilst the use of just $AlCl_3$ gives the *l* isomer exclusively. The second step is as one would expect dependent upon the chain length of the acetal stannane. For (**1**) the new ring junction formed is exclusively *cis* in all cases whilst the six and seven-membered rings are formed as a mixture of *cis* and *trans* isomers with the *trans* predominating in both cases[5].

Finally the process can be extended to reaction with carbohydrate derivatives such as the glycal (**3**). Annulation reactions on carbohydrates are rare[6] but as shown below we form the fused derivative in a stereocontrolled manner but in modest yield since the second step of the process requires the use of $AlCl_3$ resulting in reduced yields for this process.



(3)

35%

+ (1)

i,TMSOTf; ii,$AlCl_3$

REFERENCES AND NOTES

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2. Mukaiyama, T, Wariishi, K, Saito, Y, Hayashi, M, Kobayashi, S; *Chemistry Letters*, **1988**, 1101.
3. Lee, T.V, Boucher, R.J, Ellis, K.L, Richardson, K.A; *Tetrahedron Letters*, **1988**, 29, 685.
4. Lee, T.V, Ellis, K.L, Richardson, K.A; Visani, N, *Tetrahedron*, **1989**, 45, 1167.
5. All new compounds gave satisfactory analytical and/or spectroscopic data. Additionally high-field nmr (400MHz) allows the ready assignment of the diastereoisomers formed in these reactions (including the ratio of *l* to *u*) as will be reported in a full account of this work.
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