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Heteroatom-Stabilized Allylic Cations in 4+3 Cycloadditions. A Tandem Peterson Olefination/4+3 Cycloaddition Reaction

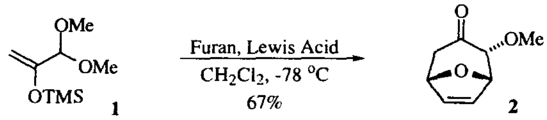
Michael Harmata* and Darin E. Jones

Department of Chemistry, University of Missouri-Columbia, Columbia, Missouri 65211

Summary: The readily available tertiary alcohols **4a-c** react with selected dienes in the presence of titanium tetrachloride to give 4+3 cycloaddition products. The process is best rationalized as a Peterson olefination followed by allylic cation formation and 4+3 cycloaddition. © 1997 Elsevier Science Ltd.

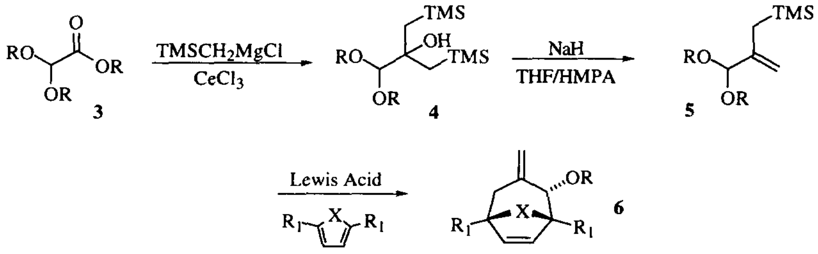
The 4+3 cycloaddition reaction between allylic cations and dienes is a powerful, convergent approach to the synthesis of seven-membered rings.[1] Of the many routes for the preparation of allylic cations for use in this reaction, only a few involve heteroatom-stabilized systems, in which at least one of the heteroatoms is an element other than a halogen.[2]

Given the large amount of acetal chemistry developed for the purpose of carbon-carbon bond formation, it would appear that allylic acetals could be of unique significance in the development of the 4+3 cycloaddition reaction.[3] Indeed, Albizati and Murray have reported that the acetal **1** could serve as a progenitor of an allylic cation (or its equivalent) in intermolecular 4+3 cycloaddition reactions as illustrated in equation 1.[2a]



(1)

We sought to develop this kind of chemistry further and are particularly interested in the use of chiral acetals and chiral catalysts to effect asymmetric induction. To that end, we recently reported that the reaction of acetals such as **5** with various dienes could give rise to 4+3 cycloadducts in good to excellent yields (Scheme 1).[4]

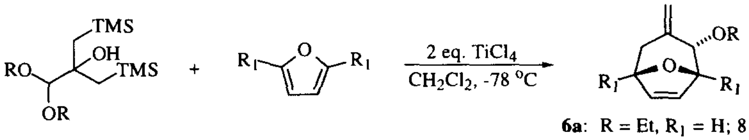


Scheme 1

The synthesis of acetals such as **5** involved the addition of trimethylsilylmethylmagnesium chloride in the presence of cerium chloride to esters of glyoxylic acid acetals followed by a base-induced Peterson olefination reaction.

We reasoned that since the Peterson olefination could also be effected under acidic conditions,[5] treatment of the alcohols such as **4** with a Lewis acid in the presence of a diene could give rise to 4+3 cycloadducts. This report details the successful implementation of that concept.

The results of our initial study are summarized in equation 2. Treatment with a 0.1 M solution of **4** in dichloromethane with 1.5 equivalents of diene followed by 2 equivalents of $TiCl_4$ at -78 °C gave 4+3 cycloadducts in fair to good yields as single stereoisomers. It is important to note that the yields obtained are lower, but not significantly so, from those obtained when the corresponding allylic acetals are used as starting materials. The stereochemistry of the cycloadducts was assigned based on NMR studies in accord with precedent.[2a,4] Unfortunately, cyclopentadiene, in contrast to its reactions with **5**, failed to give cycloadducts under these conditions.



4a: R = Et
4b: R = Me
4c: R = iPr

6a: R = Et, R$_1$ = H; 81%
6a$_1$: R = Et, R$_1$ = Me; 47%
6b: R = Me, R$_1$ = H; 53%
6b$_1$: R = Me, R$_1$ = Me; 44%
6c: R = iPr, R$_1$ = H; 48%

(2)

The full scope of this process and its possible application to chiral acetals remain to be ascertained. New results will be reported in due course.[6]

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References and Notes

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6. All new compounds exhibited satisfactory ^{1}H and ^{13}C NMR and IR spectral data as well as satisfactory combustion analysis or exact mass data.

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