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Stereospecific Allylation of "Ribo" and "Galacto" Aldosulose Derivatives

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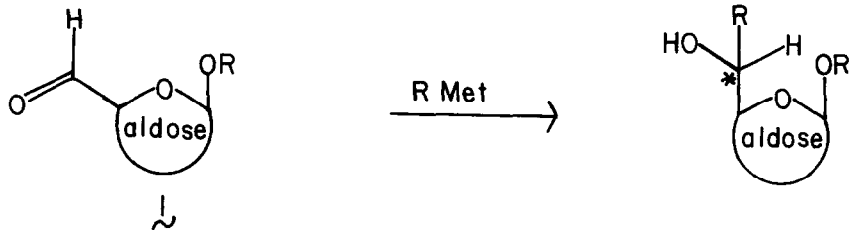
Summary: By varying the nature of the Lewis Acid catalyst in the Sakurai reaction, highly selective allylation of the side chain aldehydes can be achieved.

With few exceptions, reactions of organometallic reagents with aldosuloses of the type **1** have not exhibited high margins of stereoselectivity.[1] This lack of control complicates the extension of the asymmetric biases of pyranose or furanose templates to more extended systems.



We have recently found[2] that diastereofacial selectivity in the Felkin (Cram)[3] sense is often greater when addition of the carbon nucleophile is fostered by Lewis Acid catalysis. This phenomenon has been generalized and interpreted by Heathcock and co-workers.[4a] Accordingly, the reactions of aldehydes **2** and **3** with allyltrimethylsilane under Lewis Acid catalysis were investigated. It was hoped such a Sakurai[5] process would afford high Felkin-Cram selectivity. This hope was realized.

Reaction of the silane with aldehydes **2** or **3** in methylene chloride at -78° C under catalysis by $BF_3 \cdot OEt_2$ was highly selective, affording compounds **4** and **6** (apparent Felkin-Cram products)[3,6] in high diastereofacial excess, relative to stereoisomers **5** and **7** (apparent chelation-control products). **Conversely, when the reaction was carried out in the same solvent at the same temperature with catalysis by $TiCl_4$, stereoisomers 5 and 7 predominated substantially.**[6] This preference presumably arises from chelation of a titanium specie between the carbonyl and ring oxygens. Similar results have been noted by Reetz,[1i] by Keck,[7] and by Heathcock[4b] in related, but simpler systems. As expected by analogy,[1] the corresponding reactions with allylmagnesium bromide with each aldehyde exhibited poor selectivities.

The excellent access to compounds **4-7** is proving to be quite helpful in the stereospecific synthesis of a variety of biologically important natural products. The results of these efforts will be described in due course.

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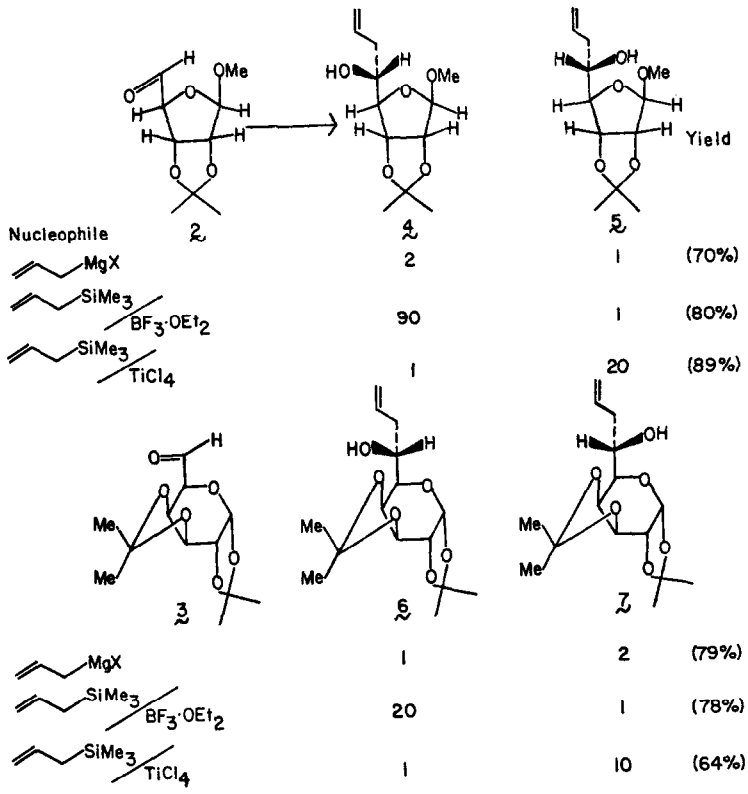

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