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Synthesis of -2-deoxy-ulosides by Michael addition of hex-1-en-3-ones

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Objective:

In our synthetic efforts, we present herein a new synthetic method preparing -2-deoxyulosides by Michael additions of various alcohols to hex-1-en-3-ones. Particularly, several Lewis bases and solvents were examined to obtain satisfying yields and stereoselectivity.

Materials and methods:

Hex-1-en-3-ones 1 and 2 that were prepared from fully protected endo-glucals, first reacted with n-octanol under basic conditions. Several Lewis bases (3.0 equiv) were examined (Table 1), including sodium hydroxide, 1,8-diazabicyclo[5.4.0]undec-7-ene, potassium carbonate , potassium tert-butoxide, and 4-dimethylaminopyridine. The reactions were carried out in dichloromethane at room temperature for 0.5h. Among these reactions shown in Table 1, NaOH was found to provide the desired product n-octyl-2-deoxy- -deoxyulosides with the highest isolated yield (75%) and stereoselectivity (ratio of ~ -anomers: 90/10). It is noted that the amount of NaOH can be reduced to 1.0 equiv, but the reaction needs longer time (2 h) for completion.Meanwhile, a variety of solvents were examined, including DMSO, DMF, THF,1,4-dioxane, CH2Cl2, toluene, and benzene. Interestingly the reactions in nonpolar solvent (e.g.,benzene and toluene) were found to afford higher yields and stereoselectivities, in contrast to those in polar solvent (e.g., DMSO and DMF). As a result, the optimal condition is to carry out the reaction in benzene in presence of NaOH.

Results:

-2-Deoxyulosides were synthesized in moderate to good yields by Michael addition of various O-nucleophiles to hex-1-en-3-ones in the presence of NaOH. These glycosyl additions were complete in 30 min at room temperature with high -stereoselectivity in 53-92% yield. In addition, high -stereoselectivity was also observed when S-nucleophiles were examined at 0℃ for 90 min.

Conclusion:

Hex-1-en-3-ones were successfully converted to -2-deoxy-ulosides by reacting with various O- and S-nucleophiles in the presence of NaOH via Michael addition. In comparison with previous procedures, this new developed method led to excellent yields and great -stereoselectivity.