



Synthesis of Optically Sugar Alcohols by Diastereoselective Addition of Organozinc Reagents

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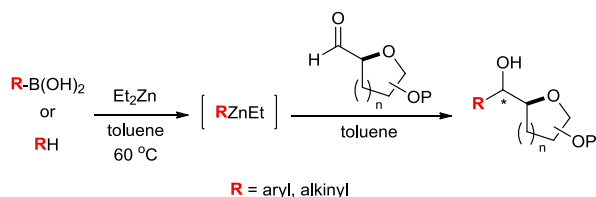
INTRODUCTION

Enantioselective addition of organometallic reagents to aldehydes affords optically active secondary alcohols, components of many naturally occurring and biologically active compounds. Moreover they are also important as synthetic intermediates of various functionalities.¹

Mixed organozinc reagents have played an important role, especially because of its low reactivity, which makes them suitable for the use in asymmetric catalysis.² Considering our interest on the use of carbohydrates as starting material for the synthesis of chiral molecules, and the peculiar reactivity pattern of organozinc reagents, particularly of type Zn-alkynyl-Alkyl and Zn-Aryl-Alkyl, in this report we present: The preparation of optically active secondary alcohols from diastereoselective addition of organozinc reagents to aldehydes obtained from sugars (*D*-mannitol, *D*-ribose and *D*-glucose).

RESULTS AND DISCUSSION

Since the starting materials appropriately synthesized,^{2,3} two studies were made on diastereoselective addition reactions: alkynylation and arylation of sugar aldehydes (Scheme 1).



Scheme 1. General approach for the diastereoselective addition of sugar-derived aldehydes.

The **alkynylation** reaction of sugar aldehydes was studied using an alkynylzinc reagent generated *in situ* by the deprotonation of phenylacetylene (1.2 equiv.) with diethylzinc (3.5 equiv.). The resulting alkynylalkylzinc reagent reacted with sugar aldehydes (1 mmol), and the corresponding optically active alcohols were formed. After screening of solvents, optimization of temperature and reaction time led us to our best conditions for the aryl transfer reaction, and the results are described in the **Table 1, entry 1-2**. Despite several attempts to improve the observed stereoselectivity, we were not able at this point to achieve high levels of

diastereoselectivity. The initial studies for the **arylation** reaction were focused on optimization of the reaction conditions using phenylboronic acid and aldehyde derived from *D*-mannitol (1 mmol). The arylzinc reagents were prepared *in situ* by a boron-zinc exchange using phenylboronic acid (1.2 equiv) and diethylzinc (7.2 equiv.). The optimized reaction conditions led us to our best conditions for the aryl transfer reaction (toluene as the solvent, 0 °C, 3h), in which the desired product was obtained in modest 30% yield and an good diastereoisomeric ratio of 11:1 (**Table 1, entry 3**).

Table 1. Diastereoselective addition of sugar-derived aldehydes.

#	aldehyde	product / cond.	yield (%) ^a	dr ^b
1	<i>D</i> -glucose	 25 °C, 3 h	64	4.5:1
2	<i>D</i> -glucose	 25 °C, 4 h	51	2.4:1
3	<i>D</i> -mannitol	 0 °C, 3h	30	11:1
4		 -20 °C, 4h	50	9.3:1

^a Isolated yields. ^b Determined by ¹H NMR.

CONCLUSION

Our results are close to success by observing the capacity this sugars aldehydes structures to convey the chiral imprint of the ring to new side chains formed. Further efforts to expand the reaction to other substrates are under investigation.

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