Stereospecific access to α-hydroxycarboxylic acids: chiral pool approach using arabinose and galactose. Preliminary results.

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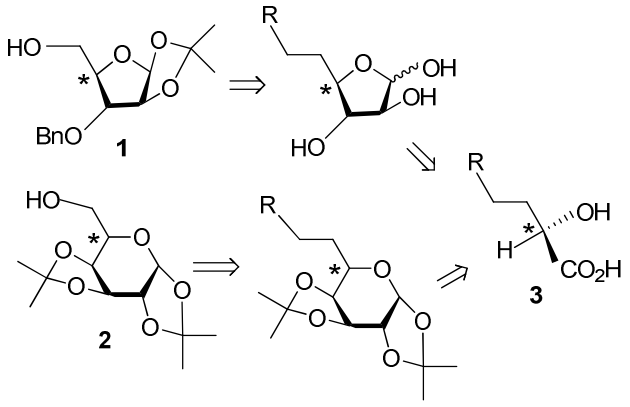
INTRODUCTION

Carbohydrates are well-known substrates for stereoselective chiral pool synthesis, due to their known absolute configurations and developed methodology of selective manipulation of the –OH groups. Since both enantiomeric final products are sometimes necessary, D- and L- sugars should be available. Since D- and L-arabinose are easily available, we concentrated attention on them to obtain general building blocks for α-hydroxycarboxylic acids synthesis. Alternatively, D-galactose was used considering a fact, that it can be converted to its L-enantiomer. Consequently, both approaches are stereospecific.

RESULTS AND DISCUSSION

Logic of chirality utilization throughout the present work is shown in the **Picture 1**.

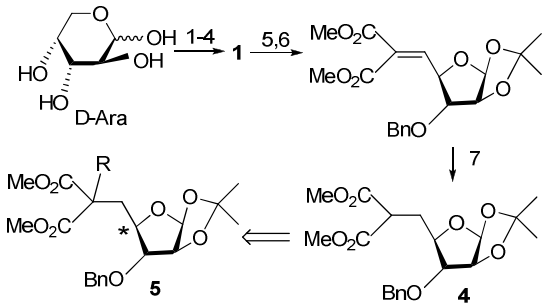


Picture 1. Utilization of chirality of the C4 and C5 atoms in **1** and **2**, respectively, to get α-hydoxycarboxylic acids.

D-Arabinose was converted to its derivative **1** and further worked-out as shown in the **Scheme 1** to get a critical intermediate **4**, which will be used to obtain **5** and eventually the targets **3.** It should be pointed out that repetition of the same scheme using L-arabinose will allow obtention of the enantiomeric targets, and in fact we already have an enantiomer of **1** derived from L-Ara.

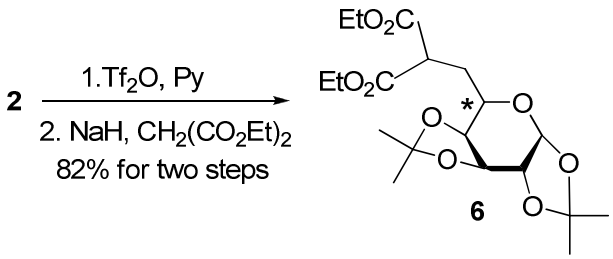
An alternative approach to **3** is to use D-galactopyranose **2** as shown in the **Scheme 2**.

Apparently simple substitution at the primary position in **2** is troublesome. Using the best leaving group, a trifluorosulfonate, smooth substitution with sodiomalonate was realized to get **6**. The structure of this compound was confirmed by X-ray.[1] Alkylations at the acidic C atom in **4** and **6** are in progress.



Conditions: 1. *t*BuPh$_2$SiCl, imidazole, 58%; 2. *acetone,* H_2SO_4, *67%*
3. BnBr, PTC, 83%; 4.Bu_4NF, 72%; 5.$NaNO_2$, Ac_2O
6.$CH_2(CO_2Me)$, MeO^-Na^+, 55% two steps; 7.NaBH4, 71%

Scheme 1. Synthesis of the intermediate **4** starting from D-arabinose.



Scheme 2. Synthesis of the intermediate **6** via substitution at the C6 of D-galactopyranose.

CONCLUSION

D-Arabinofuranose and D-galactopyranose were functionalized to get the intermediates for α-hydroxycarboxylic acids synthesis.

REFERENCES

[1] Doboszewski, B.; Silva, P.R. da; Nazarenko, A.Y.; Nemykin, V.N. *Acta Cryst.***2010**,E*66*,3217