Stereospecific obtention of building blocks for β-hydroxycarboxylic acids: D- and L-arabinose approach

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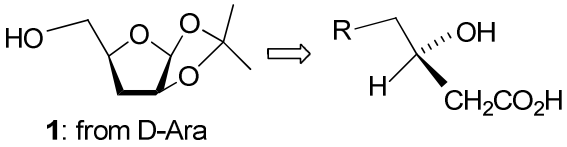
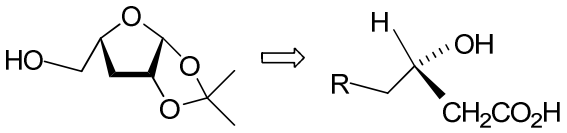
INTRODUCTION

The Lipids A, constituents of the lipopolysaccharides from the outer membrane of Gram-negative bacteria are highly toxic and potentially lethal via overactivation of the immune system.[1,2] However, in the case of cancer or AIDS patients, immune activation can be beneficial. One can therefore consider analogs of the Lipids A as potential immunity boosters without their toxic character. Since β-hydroxycarboxilic acids are one of the components of Lipids A, their general synthesis in chiral forms for further work is desired. Reported here is a stereospecific synthesis of the chiral building blocks **1** and **2** which permit obtention of the β-hydroxycarboxylic acids of variable moiety R.



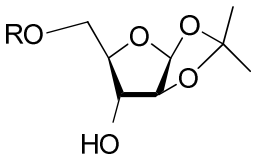
1: from D-Ara



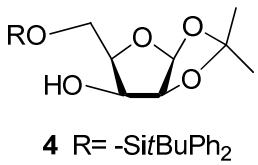
2: from L-Ara

RESULTS AND DISCUSSION

Our approach takes advantage of availability of D- and L-arabinose, their reasonable price and their stereochemical constitution. In its furanoses form, e.g. **3**, D-arabinose exposes a free –OH group amenable for removal. Attempts to apply Barton-type deoxygenation to get **1** starting from either **3** or the *lyxo* compound **5** (obtained from **3** via oxidation and reduction) proceeded in low yields (ca 25%). Excellent yields however were obtained during treatment of 3-O-triflate derived from **4** with $LiHBEt_3$.

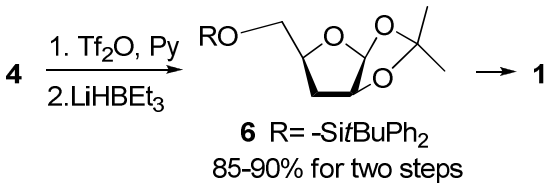


3 R= -Si*t*BuPh$_2$



4 R= -Si*t*BuPh$_2$

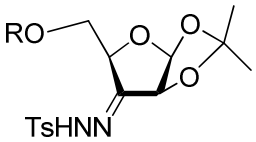
5 R= H



Scheme 1. Exceptionally efficient deoxygenation in **4** *via* substitution using "superhydride" $LiHBEt_3$

The procedure shown above was applied to 5-O *t*butyldiphenylsilyl-1,2-isopropylidene- L-arabinofuranose to furnish enantiomeric compound **2**.

Attempts are underway to transform **7** to **1** via a modified Wolff-Kishner reaction.



7 R= -Si*t*BuPh$_2$

CONCLUSION

Efficient chiral pool stereospecific procedure was devised to obtain building blocks for synthesis of β-hydroxycarboxylic acids.

ACKNOWLEDGEMENTS

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REFERENCES

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[2] Carbohydrates in chemistry and biology. Ernst, B.; Hart, G.W.; Sinaÿ, P., eds. Wiley-VCH, 2000.