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-hydroxycarboxylic 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 \(R\).

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 \(\text{f}x\)xo 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 LiHBEt3.

\[ \text{HO} \quad \text{O} \quad \text{O} \quad \text{OH} \quad \text{CH}_2\text{CO}_2\text{H} \quad \text{H} \]

1: from D-Ara

\[ \text{HO} \quad \text{O} \quad \text{O} \quad \text{OH} \quad \text{CH}_2\text{CO}_2\text{H} \quad \text{H} \]

2: from L-Ara

3 \( R = \text{SítBuPh}_2 \)

4 \( R = \text{SítBuPh}_2 \)

4 \( R = \text{H} \)

\[ \text{RO} \quad \text{O} \quad \text{O} \quad \text{H} \quad \text{CH}_2\text{CO}_2\text{H} \]

6 \( \text{R} = \text{SítBuPh}_2 \)

85-90% for two steps

\[ \text{1} \quad \text{2} \quad \text{LiHBEt}_3 \]

\[ \text{TsHNN} \]

7 \( \text{R} = \text{SítBuPh}_2 \)

CONCLUSION

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

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REFERENCES