ABSTRACT

Biomimetic Synthesis of Chiral Cyanogenic Glycosides

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A mixture of α- and β- glycosides of 2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosylmandelonitrile **19.1** was successfully synthesized from 2,3,4,6-tetra-*O*-benzyl-1-*O*-1,3,2-dioxaphosphacyclohexane-α,β-D-glucopyranosyl-2-oxide **16.6** and *O*-(trimethylsilyl)mandelonitrile **18.3** in 73% yield, where the *O*-(trimethylsilyl)mandelonitrile **18.3** was synthesized by Kobayashi's[17] procedure from benzaldehyde **18.1** and trimethylsilyl cyanide **18.2**.

Having synthesized a mixture of α- and β- cyanogenic glycoside **19.1** we were then successful in synthesizing *R*-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylmandelonitrile **21.5**, a chiral cyanogenic glycoside from 2,3,4,6-tetra-*O*-acetyl-1-*O*-1,3,2-dioxaphosphacyclohexane-α,β-D-glucopyranosyl-2-oxide **21.3** and the chiral cyanohydrin, mandelonitrile **21.4** in a yield of 72%.

The use of 1,3-diylphosphate activation of the glucose ring for the glycosylation reaction allowing the desired *β*-glycoside where the acetyl protecting group is used, provides an alternative means for the synthesis of these cyanogenic glycosides.

Having successfully synthesized a chiral cyanogenic mono-glycoside the synthesis of a cyanogenic di-glycoside, amygdalin **24.6** was next envisioned. Acetyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside-(1→6)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside **23.3** was synthesized from acetyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside **23.2** and 2,3,4,6-tetra-*O*-acetyl-1-*O*-1,3,2-dioxaphosphacyclohexane-β-D-glucopyranosyl-2-oxide **21.3** in 53% yield. The synthesis of this protected gentiobiose disaccharide **23.3** will ultimately lead to the synthesis of amygdalin **24.6**.

A chiral cyanogenic di-glycoside, *R*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl-mandelonitrile **24.5**, was also synthesized from its precursor sugar, 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-1-*O*-1,3,2-dioxaphosphacyclohexane-β-D-glucopyranoside **24.4**, in an overall yield of 41%. The use of 1,3-diylphosphate activation of the lactose ring for the glycosylation reaction allowing the desired *β*-di-glycoside was also utilized in this synthesis.

Future work involves the completion of the synthesis of amygdalin (Scheme **24**) and the synthesis of a chiral catalyst that would enable the synthesis of a wide variety of chiral cyanohydrins resulting in the synthesis of different chiral cyanogenic glycosides. The catalyst that would be chosen is the Jacobsen's[22] catalyst **25.3** which is synthesized from 2-isothiocyanato-3,3-*N*-trimethyl-butyramide **25.1** and *N,N*-diisopropyl-cyclohexane-1,2-diamine **25.2**.

Keywords: Chiral cyanohydrin; Mandelonitrile; 1,3-diylphosphate activation of the glucose ring; Amygdalin; Jacobsen's catalyst.