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## 4-O-TfO-2,3-anhydro- $\beta$ -L-ribopyranosides as Chiron : A Formal Synthesis of Canadensolide

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**Abstract.** A methodology for the preparation of densely functionlized  $\gamma$ -Butyrolactones from 2,3-anhydro pentopyranosides is described. Copyright © 1996 Elsevier Science Ltd

Carbohydrate-based syntheses generally revolve around the efficient preparation of branched chain monosaccharides. We have recently shown that 4-O-trifloxy-2,3-anhydropentopyranosides (1) are attractive chirons, since they may be obtained on multi-gram scale from common pentoses, and easily converted to 4-C-branched derivatives.<sup>1</sup> The latter appear to be especially appropriate precursors for the synthesis of highly oxygenated butyro- $\gamma$ -lactone (scheme 1). Herein, we illustrate this methodology by application to the preparation of the densely functionlized, antibiotic, canadensolide (4).<sup>2</sup> Three syntheses of this target have been reported but are relatively lengthy and low yielding.<sup>3-6</sup>





Retrosynthetically, canadensolide may be derived from the monocyclic butyro- $\gamma$ -lactone **3** thence the 4-C-pentopyranoside **2**. This pivotal, branched chain sugar contains all the required stereogenic centers and is primed for elaboration to canadenosolide (scheme 1).

Thus, benzyl 4-O-trifloxy-2,3-anhydro- $\beta$ -L-ribopyranoside (1) was transformed via reaction with the lithium salt of t-butylacetate to the 4-C-derivative 2, which on treatment with trifluoroacetic acid gave the fused pyranobutyro- $\gamma$ -lactone (5) in 87% overall yield from 1.<sup>1</sup> Hydrogenolysis of 6 afforded the lactol 3, the pyranose tautomer of the hydroxyaldehyde 3.

Wittig reaction of **6** using propyl triphenylphosphoniumbromide and potassium *tert.*- butoxide in dry THF at room temperature for 30 min and then at 80°C for 20 min afforded an E/Z mixture of alkenes **7** in 58% yield.<sup>7</sup> Hydrogenation of **7** followed by Swern's oxidation of the reduced product afforded lactol **8**.<sup>8,9</sup> Since **8** has been previously transformed over three steps to canadenosolide, this constitutes a formal synthesis.



Scheme 2. Reagents and conditions: i) H<sub>2</sub>/ Pd(OH)<sub>2</sub>/ C (93%); ii) C<sub>2</sub>H<sub>5</sub>CHPPh<sub>3</sub>\*Br<sup>-</sup>/ K'BuO (58%); iii) H<sub>2</sub>/ Pd/ C (87%); iv) Ac<sub>2</sub>O/ DMSO (63%).

The synthesis of **8** is considerably more practical than previous approaches. It involves a straightforward six step sequences in a good overall yield (26%) from benzyl 4-O-trifloxy-2,3-anhydro- $\beta$ -L-ribopyranoside (1), a precursor which is available on 20 g scales. Moreover, the potential of the fused pyrano- $\gamma$ -lactone **5** as a versatile intermediate for the preparation of the ubiquitous butyro- $\gamma$ -lactone framework has been demonstrated.

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