Stereodivergent Synthesis of Decahydroquinoline-Type Poison Frog Alkaloids -Part 1-

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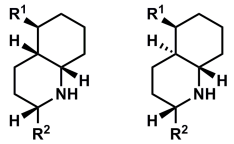
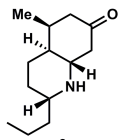
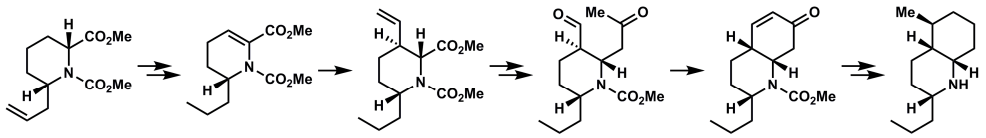


Figure 1.

Neotropical poisonous frogs are a rich source of a structurally diverse array of alkaloids. Among them, the 2,5-disubstituted decahydroquinolines are one of the major classes of these amphibian alkaloids. In addition, these alkaloids contain both *cis*- and *trans*-fused decahydroquinoline nuclei having the diastereomeric centers at C-2 and C-5 positions (Figure. 1). However, no methodology for the stereodivergent synthesis of the *cis*- and *trans*-fused ring systems has been reported to date. We herein describe the stereoselective and stereodivergent route to the *cis*- and *trans*-fused decahydroquinoline ring core.

The synthesis began with known allyl derivative **1**, which was converted to enaminoester **2**. The key Michael-type of conjugate addition reaction of **2** proceeded smoothly to give rise to the trisubstituted piperidine **3** as a single isomer, which was converted to Weinreb's amide. The Weinreb's amide was transformed into the keto aldehyde **4**, which was subjected to an intermolecular aldol type of cyclization to afford the enone **5** as a single isomer. The methyl group was introduced on the C-5 position of **5** with highly stereoselective manner. Barton's deoxygenation of the resulting ketone followed by deprotection of methoxycarbonyl group provided ***cis*-195A** (Scheme 1).





Scheme 1.

On the other hand, the *trans*-fused compound **6** was also synthesized starting from the common Weinreb's amide. The conversion of **6** to ***4a-epi-cis* 195A** is now in progress and will be reported.