Stereodivergent Synthesis of Decahydroquinoline-Type Poison Frog Alkaloids -Part 2-

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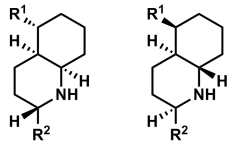
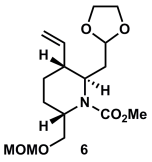
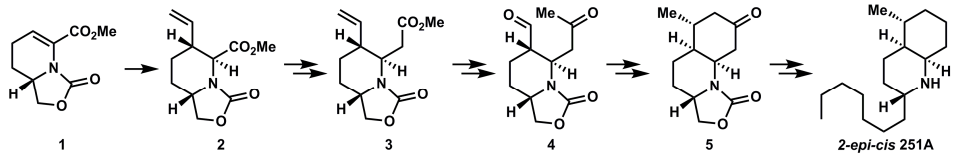


Figure 1.

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 enaminoester **1**, which was converted to the adduct **2** using the key Michael-type of conjugate addition reaction as a single isomer. The adduct **2** was transformed into the homologated ester **3**, which was converted to keto aldehyde **4**. The second key step was an intermolecular aldol type of cyclization of **4** to afford the enone as a single isomer, which was introduced the methyl group on the C-5 position to afford the quinoline **5** with highly stereoselective manner. Barton's deoxygenation of the resulting ketone followed by hydrolysis of oxazolidinone ring provided amino alcohol, which was converted to ***2-epi-cis* 251A** in 4 steps (Scheme 1).





Scheme 1.

On the other hand, the *trans*-fused compound **6** was also synthesized starting from the common homologated ester **3**. The conversion of **6** to ***trans* 195A** is now in progress and will be reported.