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

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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).

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.