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Total syntheses and their biological evaluation of poison-frog alkaloids ent-cis-195A and cis-211A

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To date, over 800 lipophilic alkaloids representing more than 20 structural classes have been detected from the skin extracts of neotropical poison frogs. The 2,5-disubstituted decahydroquinolines are represented one of the major classes, and the structural diversity and pharmacological activity associated with this class of alkaloids have stimulated synthetic activity in numerous groups. We report here the first total synthesis of the decahydroquinoline type poison-frog alkaloid cis-211A along with ent-cis-195A. The synthesis began with known piperidine 16, which was converted to aminoester 2 in 3 steps. Michael-type conjugate addition reaction of 2 provided the adduct 3 in high yield as a single stereoisomer. The ester 3 was transformed into the keto-aldehyde 4, which was subjected to an intermolecular aldol-type cyclization to afford the cis-fused enone 5 as a single isomer. The conjugate addition reaction of 5 followed by treatment of the resulting enolate with Comins' reagent gave rise to the common and key intermediate of enol triflates 6. Synthesis of ent-cis-195A was achieved from 6 in 2 steps, and the first total synthesis of cis-211A was also completed from 6 in 5 steps as shown in Scheme1. Details of the synthetic process synthesis and their evaluation of the nicotinic acetylcholine receptors and inhibitory effect on [3H] nicotine uptake by TR-BBB13 cells of both synthetic alkaloids will be reported.



Figure 1. Chemical structure of c/s-195A and 211A

Biography

Naoki Toyooka has done B. S. in Pharmaceutical Sciences from Kinki University, March 1984. He completed his Ph. D. in Pharmaceutical Sciences from Kinki University, March 1989. He earned his Postdoctoral Research in department of chemistry from North Carolina State University with Professor Daniel L. Comins, 1997. From April 1989-March 2001 he worked as Research Associate, Toyama Medical & Pharmaceutical University. From April 2001-March 2006, he served as an Associate Professor, Toyama Medical & Pharmaceutical University. From April 2001-March 2006, he served as an Associate Professor, Toyama Medical & Pharmaceutical University. From April 2006-March 2010, he joined as an Associate Professor, University of Toyama. Currently, he is the Full Professor in University of Toyama since April 2010. Also, he is the Dean of Graduate School of Innovative Life Science, University of Toyama since April 2017.

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