Asymmetric Synthesis of Poison Dart Frog Indolizidine Alkaloids

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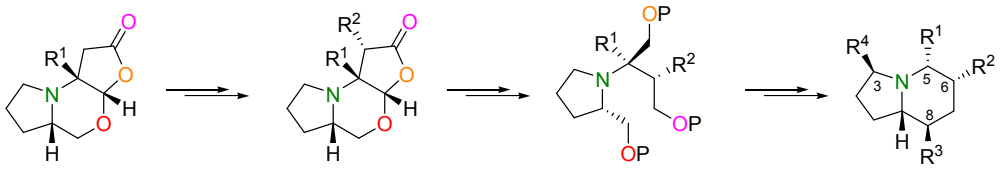
5-Substituted, 3,5-disubstituted, 5,8-disubstituted and 5,6,8-trisubstituted indolizidines belong to a group of alkaloids separated from the skin of poison dart frogs which lived in the tropical rainforest of Central and South America. Some of these indolizidines have shown interesting AChEI activity which is important for the development of new drugs.

A series of substituted indolizidines, including 167B, 195G, 209B, 209D, 209I, 223A, 223AB, synthesized starting from tricyclic lactones will be discussed. Key steps involved : 1) [3,3]-sigmatropic rearrangement to form tricyclic compounds with needed R^1 substituent, 2) asymmetric alkylation/epimerization to obtain R^2, 3) cyclization to form C7-C8 bond with R^3 in correct stereochemistry, 4) construction of R^4 (223AB case only), and 5) cleavage of the excess one carbon substituent on C5.



References:

[1] Li, Y.-J.; Chang, Y.-K.; Ho, G.-M.; Huang, H.-M. *Org. Lett.* **2009**, *11*, 4224.

[2] Li, Y.-J.; Chuang, H.-Y.; Yeh, S.-M.; Huang, W.-S. *Eur. J. Org. Chem.* **2011**, 1932.

[3] Li, Y.-J.; Hou, C.-C.; Chang, K.-C. *Eur. J. Org. Chem.* **2015**, 1659.