DIVERGENT ACCESS TO HISTONE DEACETYLASE INHIBITORY CYCLOPEPTIDES VIA LATE-STAGE CYCLOPROPANE RING CLEAVAGE STRATEGY. SHORT TOTAL SYNTHESIS OF CHLAMYDOCIN

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Cyclopeptides with histone deacetylase inhibitory (HDACi) activity remain in the spotlight of biomedical sciences as a tool for probing the mechanisms of epigenetic regulation and as promising drug candidates, including cancer therapy.We have developed a short and efficient synthesis of Aoe containing natural product Chlamydocin and related Aoda- and Asu-type inhibitory analogues (additional 9 examples) via late-stage cyclopropane ring cleavage strategy exhibiting a diversity-oriented approach and high overall yields. Due to broad spectrum of chemical transformations provided by rapidly evolving field of cyclopropanol chemistry, further advances in the last stage diversification from the single cyclopropanol precursor can be expected, suitable for the generation of bioactive molecular libraries in general and HDACi cyclopeptides in particular.

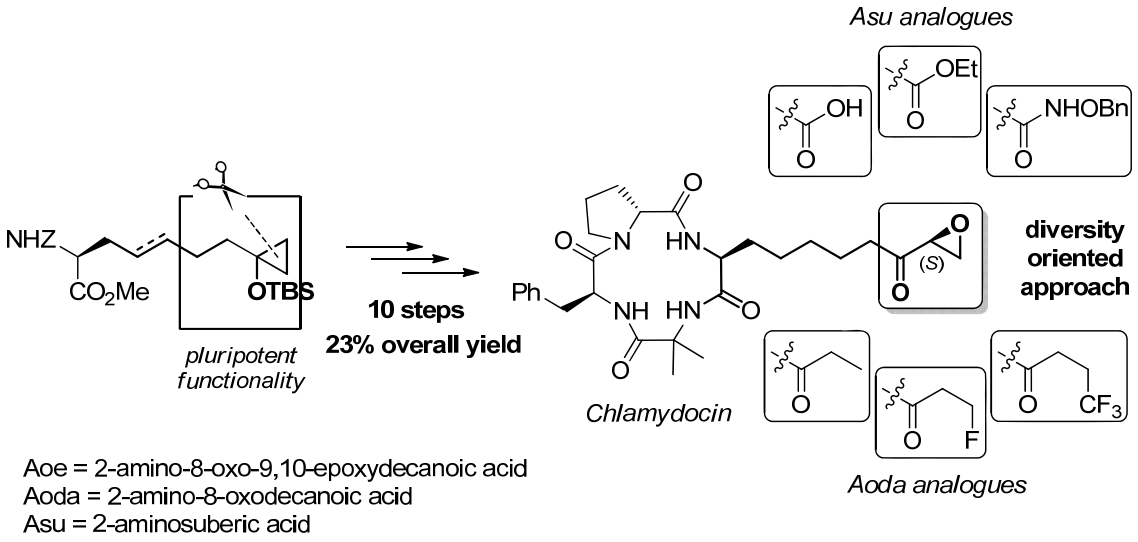

Fig.1 Synthesis of Chlamydocin and related histone deacetylase inhibitors

[1] T. L. Newkirk, A. A. Bowers, R. M. Williams, 2009, *Nat. Prod. Rep*., 26, 1293.