SHORT SYNTHESIS OF CHLAMYDOCIN AND RELATED HISTONE DEACETYLASE INHIBITORS VIA LATE-STAGE CYCLOPROPANE RING CLEAVAGE STRATEGY

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Ph
$$\frac{1}{NH}$$
 $\frac{1}{NH}$ $\frac{1}{N$

Reaction conditions: a) TBTU, NEt₃, DCM; b) aq. NaOH, then H_2 / Pd-C, 60° C, 60° C,

Fig. 1 Synthesis of Chlamydocin (7a), its epimer (7b) and related ethyl ketone compound 7c

Cyclic peptide histone deacetylase inhibitors (HDAc) have raised attention due to their application as potent antimicrobial and anticancer agents [1]. The main challenge in the synthesis of HDAc is the construction of functionalized 2-amino-8-oxodecanoic acids, crucial for bioactivity of these peptides. In our strategy, key structural fragments of HDAc are beneficially assembled at the last stage via the ring cleavage of the common cyclopropanol precursor (6), allowing to prepare a set of bioactive compounds 7a-c, as demonstrated by the short synthesis of both diastereomers of Chlamydocin (7a,b) and related ethyl ketone (7c).

References

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

