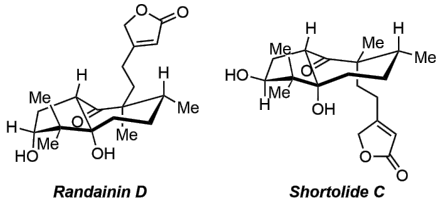
Facile access towards trans-hydroxyoctahydroazulenone core and total synthesis of diterpenoids Randainin D and Shortolide C

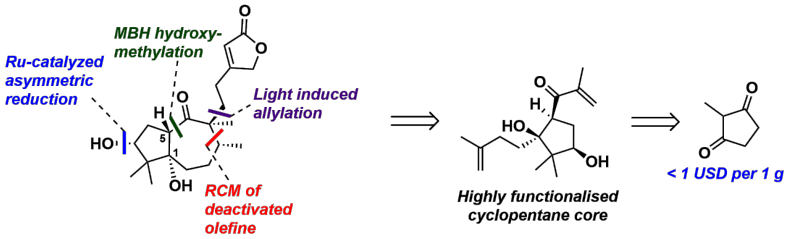
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Hydroazulene is an abundant framework found in *guaiane-type* sesquiterpenes [1]. Recently Shen [2] and Williams [3] groups isolated novel natural products (*Randainins A-D* and *Shortolides B-C*) possessing simultaneously *hydroxyoctahydroazulene* skeleton and *butenolide* moiety. Such framework features make these natural products unique, being structurally related to both, *guaiane-type* sesquiterpenes and *labdane-derived* diterpenoids. *Randainin D* is a moderate inhibitor of superoxide-anion generation and elastase release, *Shortolide C* (**Fig. 1**) reduces the growth of *Staph. aureus*. Such biological activity and intriguing structures (trans-5/7-ring scaffold, five stereocenters, four – contiguous, and two – quaternary), make these unusual natural products attractive and challenging synthetic targets.



Our goal is to develop a divergent total synthesis of *Randainin D* and *Shortolide C.* It was found that Ru-catalyzed asymmetric reduction of 2,2-dimethylcyclopentane-1,3-dione creates the stereocenter at C3, which leads to the desired trans-junction at C1-C5, through the sequence of diastereoselective steps. Assembly of the 7-membered ring was realized via challenging Ru-catalyzed RCM leading to the tetrasubstituted enone. The endgame is a novel light-induced allylation that provides access to the butenolide fragment.



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[2] Ho-Hsi Cheng, Yuan-Bin Cheng, Tsong-Long Hwang, Yao-Haur Kuo, Chung-Hsiung Chen, Ya-Ching Shen, *Journal of Natural Products*, **2015**, 78, 1823-1828.
[3] Russell B. Williams, Lin Du, Vanessa L. Norman, Matt G. Goering, Mark O'Neil-Johnson, Scott Woodbury, Matthew A. Albrecht, Douglas R. Powell, Robert H. Cichewicz, Gary R. Eldridge, and Courtney M. Starks, *Journal of Natural Products*; **2014**, 77, 1438-1444.