Total Synthesis and Structural Determination of a Marine Natural Product Callicladol with Potent Antitumor Activity against Mouse Leukemia Cells

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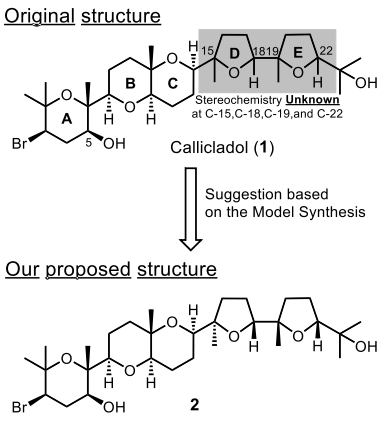
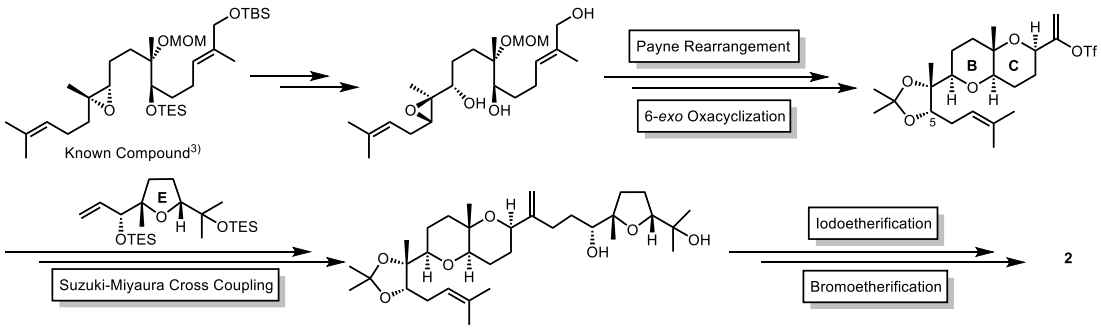
Callicladol (**1**), a marine triterpene polyether isolated from the red alga *Laurencia callicladа* by Suzuki *et al.* in 1993, exhibits potent cytotoxicity against P388 murine leukemia cell.[1] The structural features of **1** are a bromine-containing THP ring (A ring), a dioxabicyclo[4.4.0]decane ring (BC rings), and two THF rings (DE rings). It is also rare for **1** to possess a hydroxy group at the C5 position in A ring, which is unprecedented in other thyrsiferol congeners. However, due to limitations of analytical techniques, the relative configuration around DE rings in **1** remains undetermined.



Previously, we suggested the relative configuration of callicladol as shown in **2** based on the model synthesis.[2] In this work, we succeeded in the efficient construction of B ring with introduction of the C5-hydroxy group utilizing a tandem reaction *via* a Payne rearrangement followed by a 6-*exo* oxacyclization as a key step. As a result, we have achieved the first total synthesis and structural determination of callicladol.



1) M. Suzuki *et al. Chem. Lett.* **1995**, *24*, 1045.
2) The 100th CSJ Annual Meeting, Noda City, Chiba, Japan, Mar. **2020**.
3) K. Nishikibe, K. Nishikawa and Y. Morimoto *et al. Angew. Chem., Int. Ed.* **2017**, *56*, 3064.

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