Synthetic Ventures into the Furanocembranes: Bielschowskysin and Beyond

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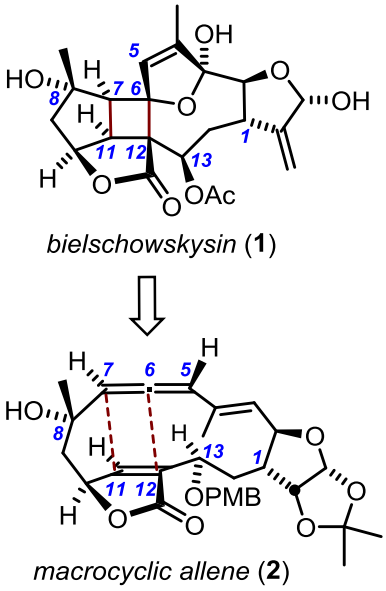
Natural products often unite chemical structure and biological function in unforeseen ways. Such facets have long driven targeted synthesis and drug campaigns. The concerted challenge for the organic chemist is not only to orchestrate a sequence of synthetic methods into a workable, clever strategy, but also to advance and develop methods and tactics in conceptually new ways.

The cembrane natural products hold such promise in both biological and chemical senses. They are a diverse class of macrocyclic diterpenes found in both plants and animals.[1] In particular, the furanocembranoids are highly oxidized cembranes, which have been discovered to exist in significant abundance and structural complexity, particularly in the *Pseudopterogorgia* sea whips from the Carribean, as well as from corals of the genus *Sinularia*, *Plumarella*, and *Leptogorgia*.[1c] Beyond their presumed antifeedant role in marine coral reefs, these biosynthetically-linked secondary metabolites display a wide range of biological activities; for example, derivatives and extracts of the pseudopterosins are not only being used medically as anti-inflammatory and analgesic agents, but are also being investigated as antimicrobial (TB, malaria) and as antitumour agents.

Bielschowskysin (**1**) belongs to this diverse class of cembranoid diterpenes.[1b] In 2006, the Rodríguez group characterized **1** to be a tricyclo[9.3.0.$0^{2,10}$]tetradecane derived from the self-closure of a regular furanocembrane macro-skeleton (about the C6/C12 and C7/C11 carbon-carbon bonds).[2] Amid several strategies from other groups, we have been striving to develop [2+2]-transannulation tactics to construct the multicyclic skeleton of **1** via macrocyclic allenes like **2** (Figure 1).[3] Previously, we secured the tricyclic cyclobutane core (C5-to-C12) of **1** by employing a stereocontrolled photochemical [2+2] cyclization of an allene-tethered γ-butenolide[3a] and have recently gained conformational insights into forming macrocyclic alkyne precursors to **2**.[3b]

In this talk, we summarise our progress to this family of natural products.[3c] In particular, we cover our macrocyclisation and transannulation strategies to the bielschowskyane framework (cf. **1**).



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