TOWARDS THE TOTAL SYNTHESIS OF PECTENOTOXIN-4

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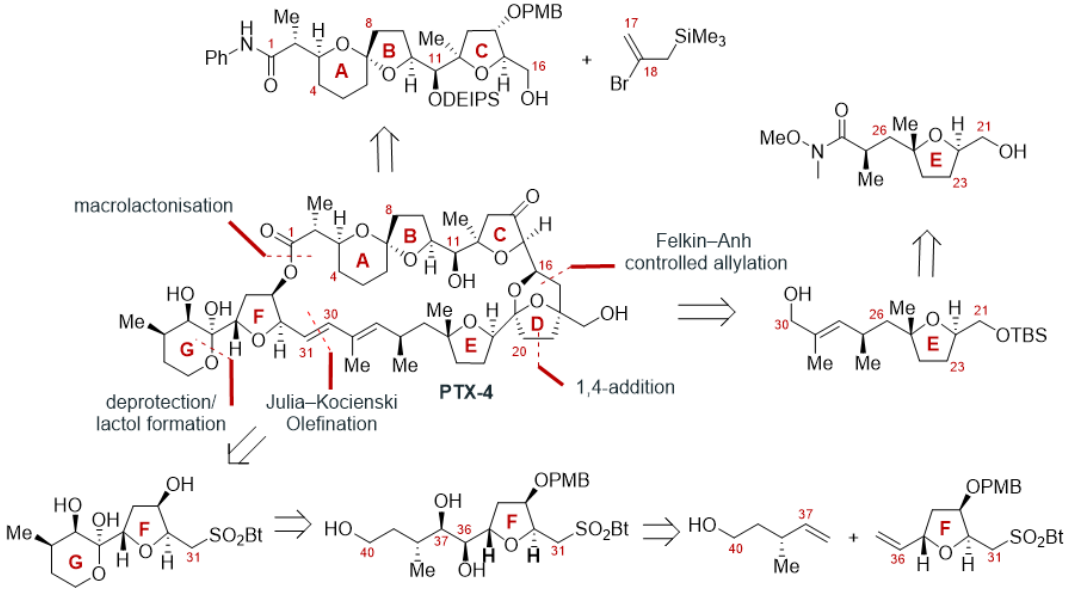
The pectenotoxins (PTXs) are a family of marine natural products first isolated by Yasumoto and co-workers in 1985 from the digestive glands of the scallop *Patinopecten yessonesis*.[1] PTXs are potently cytotoxic against several cancer cell lines, including lung, colon, CNS, melanoma, renal, ovarian, and breast cancer cell lines.[2] Their scarcity and biological activity make PTXs attractive total synthesis targets, with PTX-4 being especially desirable because it possesses a stable anomeric 6,5-spiroketal that can be subjected to a late-stage acidic equilibration to form the more potent PTX-1 and PTX-2.[3,4] It is for this reason that PTX-4 is the target for this total synthesis project.

Our retrosynthetic strategy for PTX-4 involves disconnecting the macrolide into three main fragments: C1−C16 ABC fragment **1**, C21−C30 E fragment **7**, and C31−C40 FG fragment **3**. A late-stage Yamaguchi lactonization would form the C1–C33 bond. Following that, a deprotection–lactol formation process would furnish the G ring. The C30–C31 double bond would be formed *via* a Julia–Kocienski olefination. A Felkin–Anh controlled addition of vinyl bromide **2** to the C16 aldehyde and a rhodium-catalysed conjugate 1,4-addition would connect the C and E rings. A subsequent dihydroxylation–acetalisation process would assemble the D ring.



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