CONCISE TOTAL SYNTHESES OF (–)-JORUNNAMYCIN A AND (–)-JORUMYCIN ENABLED BY ASYMMETRIC CATALYSIS

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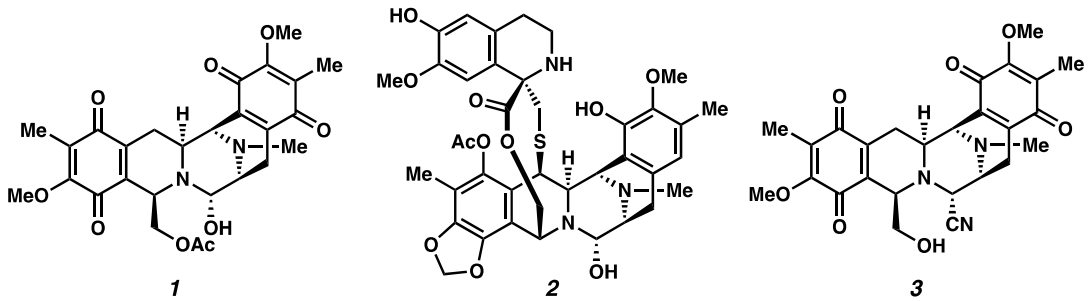
The bis-tetrahydroisoquinoline (bis-THIQ) natural products have been studied intensively over the past four decades for their exceptionally potent anticancer activity, in addition to strong Gram-positive and Gram-negative antibiotic character. Synthetic strategies toward these complex polycyclic compounds have relied heavily on electrophilic aromatic chemistry, such as the Pictet–Spengler reaction, that mimics their biosynthetic pathways. Herein, we report an approach to two bis-THIQ natural products, jorunnamycin A and jorumycin, that instead harnesses the power of modern transition-metal catalysis for the three major bond-forming events and proceeds with high efficiency (15 and 16 steps, respectively). By breaking from biomimicry, this strategy allows for the preparation of a more diverse set of nonnatural analogs.

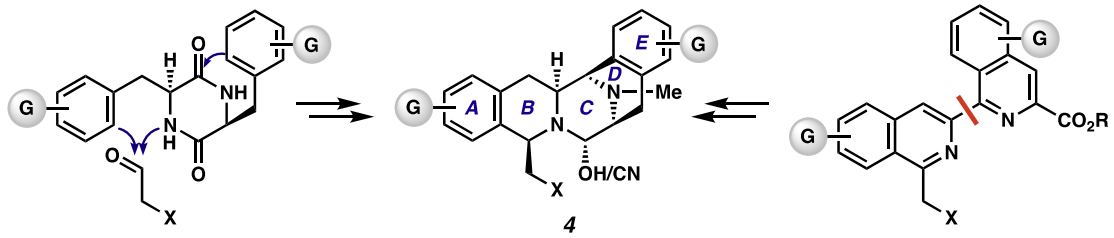
Bis-Tetrahydroisoquinoline (bis-THIQ) natural products: Alkaloids that display exceptional anticancer activity



Conventional, Biomimetic Approach: Pictet–Spengler, Bischler–Napieralski

Pentacyclic bis-THIQ Core

Our Approach (this research): Cross Coupling/Reductive Cyclization



A non-biomimetic approach will produce complementary analogs for bioactivity and medicinal chemistry studies