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Synthetic Studies of the Zoanthamine Alkaloids: The Total Syntheses of Norzoanthamine and Zoanthamine
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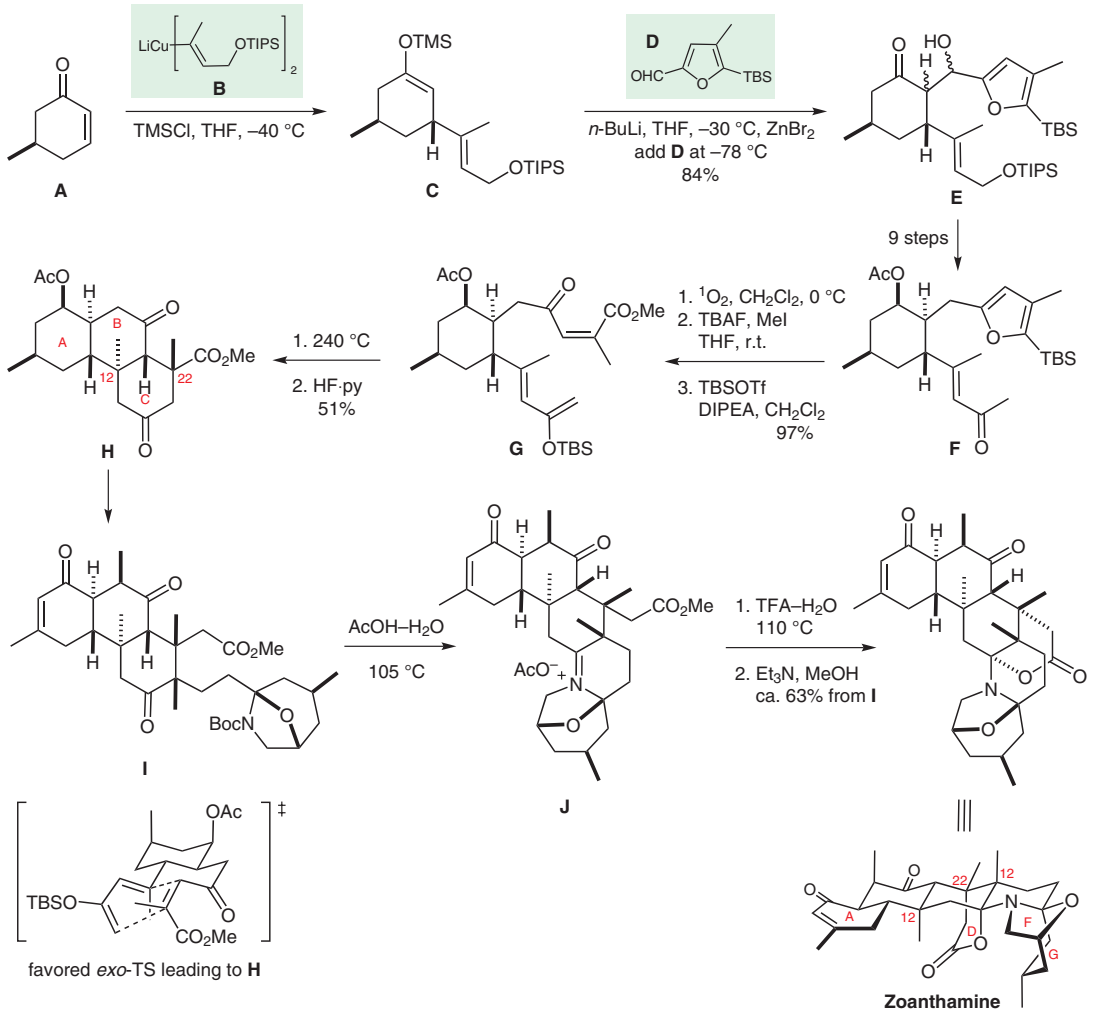
Synthesis of Zoanthamine



Significance: Zoanthamine is a marine metabolite that inhibits phorbol myristate-induced inflammation. It is also an analgesic that inhibits human platelet aggregation. Major challenges in this synthesis were (1) construction of the *trans–anti–trans* perhydrophenanthrene ABC ring system; (2) construction of the three ring C quaternary centers at C9, C12 and C22; (3) construction of the two quaternary aminal centers.

Comment: The *trans–anti–trans* ring system in intermediate **H** was constructed by an *exo*-selective intramolecular Diels–Alder reaction. Nine of the eleven stereogenic centers were created by diastereoselective reactions starting from (*R*)-5-methyl-2-cyclohexenone (**A**) and (*R*)-citronellal. The synthesis required 43 steps and proceeded in 2.2% overall yield (average 91% yield per step).

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Category
Synthesis of Natural Products and Potential Drugs

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zoanthamine
intramolecular Diels–Alder reaction
photooxidation
conjugate addition
copper