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 dia-stereoselective 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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Synthetic Studies of the Zoanthamine Alkaloids: The Total Syntheses of Norzoanthamine and Zoanthamine