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Divergent Synthesis of Natural Derivatives of (+)-Saxitoxin Including 11-Saxitoxinethanoic Acid

Total Synthesis of Saxitoxin and 11-Saxitoxinethanoic Acid

Significance: The authors report the total syntheses of (+)-saxitoxin and several structural analogues including saxitoxinethanoic acid. These bis-quinuclidinium natural products have been of high interest due to their extraordinary activity against voltage-gated sodium ion channels.

Comment: Electrophilic aromatic substitution and rhodium-catalyzed oxidative cyclization yield tricyclic system E from simple starting materials. Clever application of an Evans–Mislow rearrangement gives access to advanced intermediate F that is used to complete the synthesis of both target structures.