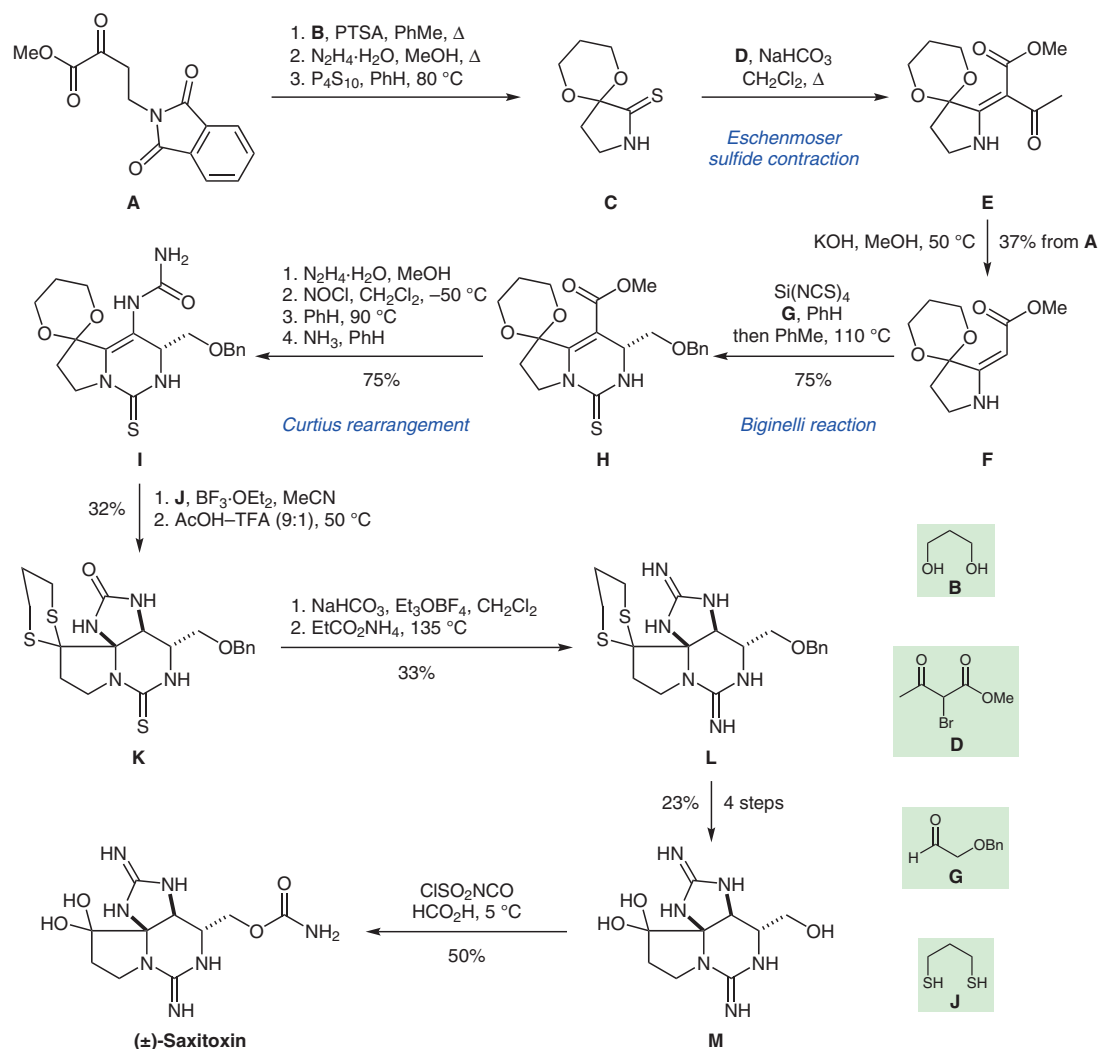


Total Synthesis of (±)-Saxitoxin



Significance: In 1977, Kishi and co-workers reported the first total synthesis of (±)-saxitoxin in 19 steps. Associated with paralytic shellfish poisoning, the potent neurotoxin was one of the most lethal non-protein substances known. The natural product features three contiguous stereocenters and a remarkably dense collection of heteroatoms with two guanidinium moieties in its tricyclic core.

Comment: Vinyllogous carbamate **F** was accessed in two steps from thionolactam **C** via Eschenmoser sulfide contraction. Biginelli reaction with silicon tetracyanate and subsequent Curtius rearrangement furnished tricyclic thiourea **I**. Deprotection of the thioketal and benzyl-ether in four steps from di-guanidine **L** gave rise to decarbamoylsaxitoxin **M**. Treatment with chlorosulfonyl isocyanate afforded the natural product.