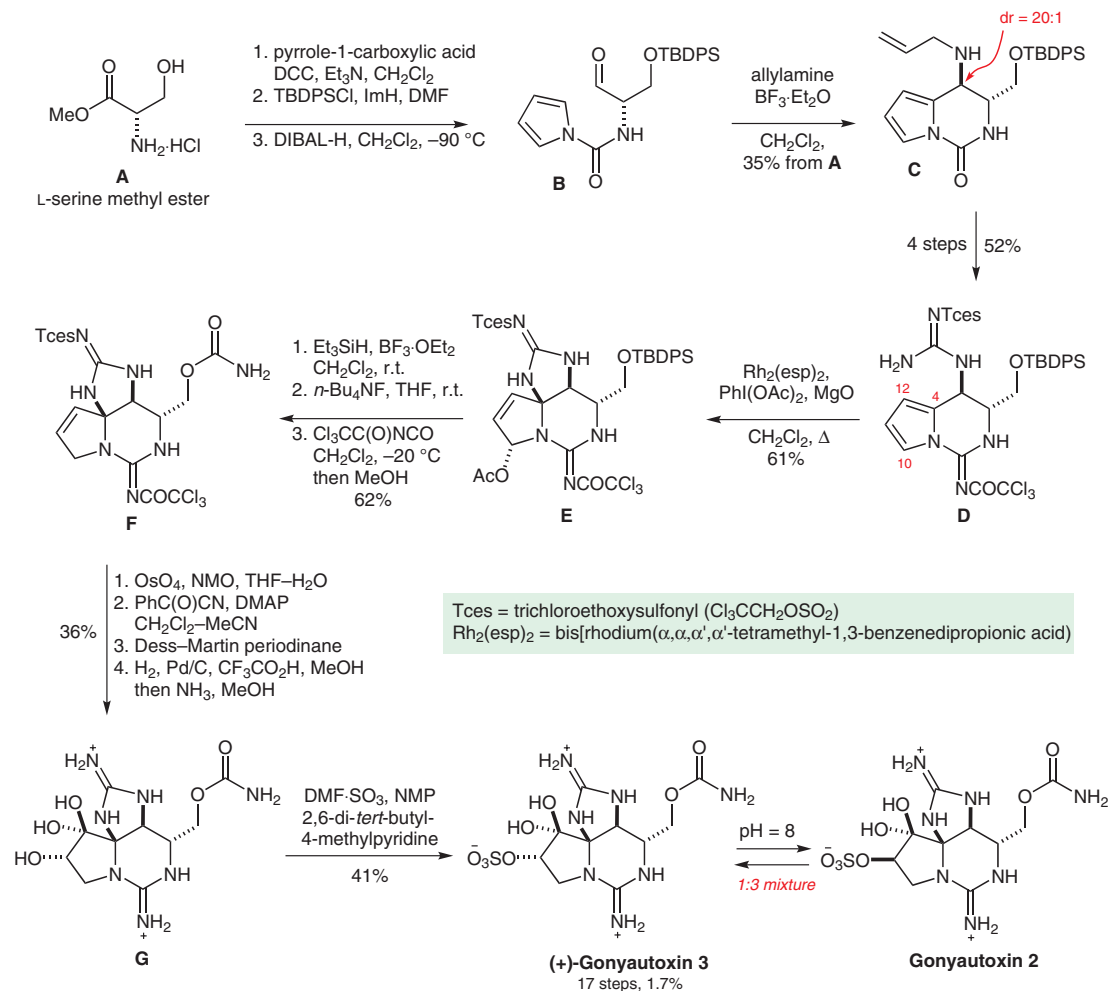


Synthesis of (+)-Gonyautoxin 3



Significance: Gonyautoxin, saxitoxin and neosaxitoxin are the major constituents of paralytic shellfish poisons. They inhibit electrical conduction in cells by acting as a stopper in ion flux through voltage-gated Na⁺ channels. The first asymmetric synthesis of gonyautoxin 3 (GTX 3) features a rhodium-catalyzed amination reaction (**D** → **E**) to access the tricyclic core of the toxin which is found in more than thirty natural products.

Comment: The amination reaction (**D** → **E**) is proposed to proceed via aziridination at C4 and C12 followed by a nucleophilic attack at C10 by acetic acid which is formed as a byproduct in the reaction. GTX 3 epimerizes to GTX 2 in aqueous acidic solution.