rhodium

sulfation



dr = 20:1 1. pyrrole-1-carboxylic acid OTBDPS **OTBDPS** DCC, Et₃N, CH₂Cl₂ allylamine 2. TBDPSCI, ImH, DMF BF₃·Et₂O 3. DIBAL-H, CH₂Cl₂, -90 °C ÑH₂⋅HCl CH2Cl2, 35% from A В L-serine methyl ester NTces 1. Et₃SiH, BF₃·OEt₂ **OTBDPS OTBDPS** CH2Cl2, r.t. Rh₂(esp)₂, PhI(OAc)₂, MgO 2. *n*-Bu₄NF, THF, r.t. HN Cl₃CC(O)NCO CH₂Cl₂, Δ CH₂Cl₂, -20 °C 61% AcO then MeOH NCOCCI3 NCOCCI₃ NCOCCI₃ 62% Ε D 1. OsO₄, NMO, THF-H₂O 2. PhC(O)CN, DMAP CH₂Cl₂-MeCN Tces = trichloroethoxysulfonyl (Cl₃CCH₂OSO₂) 36% $Rh_2(esp)_2 = bis[rhodium(\alpha,\alpha,\alpha',\alpha'-tetramethyl-1,3-benzenedipropionic\ acid)$ 3. Dess-Martin periodinane 4. H₂, Pd/C, CF₃CO₂H, MeOH then NH₃, MeOH DMF-SO₃, NMP NΗ НО HO 2,6-di-tert-butyl-HO, HO. pH = 8HO, 4-methylpyridine O₃SO Ō₃SO 41% ΝH₂ G Gonvautoxin 2 (+)-Gonyautoxin 3 17 steps. 1.7%

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 ($\mathbf{D} \to \mathbf{E}$) to access the tricyclic core of the toxin which is found in more than thirty natural products.

Comment: The amination reaction ($\mathbf{D} \to \mathbf{E}$) 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.

SYNFACTS Contributors: Philip Kocienski, Indu Dager Synfacts 2009, 5, 0467-0467 Published online: 22.04.2009 **DOI:** 10.1055/s-0028-1088173; **Reg-No.:** K03809SF